BMJ Open

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Journal:	*BMJ Open*
Manuscript ID	bmjopen-2017-017765
Article Type:	Research
Date Submitted by the Author:	16-May-2017
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Primary Subject Heading:	Health services research
Secondary Subject Heading:	Evidence based practice, Cardiovascular medicine
Keywords:	Heart failure < CARDIOLOGY, Change management < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Quality in health care < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Protocols & guidelines < HEALTH SERVICES ADMINISTRATION & MANAGEMENT

Effectiveness of implementation interventions in improving physician adherence to guideline recommendations in heart failure: a systematic review

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Keywords: heart failure, healthcare quality, change management, clinical guidelines, implementation science, knowledge translation

Word Count: 4326

ABSTRACT

Background: The uptake of guideline recommendations that improve heart failure (HF) outcomes remains suboptimal. We reviewed implementation interventions that improve physician adherence to these recommendations, and identified contextual factors associated with implementation success.

Methods: We searched databases from January 1990 - February 2015 for studies testing interventions to improve uptake of Class I HF guidelines. We used the EPOC and Process Redesign frameworks for data extraction. Primary outcomes included: proportion of eligible patients offered guideline-recommended pharmacotherapy, self-care education, left ventricular function assessment, and/or intracardiac devices. We reported clinical outcomes when available.

Results: We included 35 studies, including 9 randomized controlled trials (RCTs). Provider-level interventions (N=13 studies) included: audit and feedback, reminders, and education. Organization-level interventions (N=15) included: medical records systems changes, multidisciplinary teams, and clinical pathways. System-level interventions (N=3) included: provider/institutional incentives. Four studies assessed multi-level interventions. We could not perform meta-analyses due to statistical/conceptual heterogeneity. Twenty-nine studies reported significant improvements in at least 1 primary outcome. Clinical pathways, multidisciplinary teams, and multifaceted interventions were most consistently successful in increasing physician uptake of guidelines, while audit and feedback alone was largely ineffective. Among RCTs, pharmacist and nurse-led interventions improved target dose prescriptions. Eleven studies reported clinical outcomes; significant improvements were reported in 3, including a clinical pathway, a multidisciplinary team, and a multifaceted intervention. Baseline assessment of barriers, staff training, iterative intervention development, leadership commitment, and

policy/financial incentives were associated with intervention effectiveness. Most studies (N=18) had medium risk of bias; 8 RCTs had low risk of bias.

Conclusion: Our study is limited by the quality and heterogeneity of the primary studies. Clinical pathways, multidisciplinary teams, and multifaceted interventions appear to be most consistent in increasing guideline uptake. Our work highlights the need for improved research methodology to reliably assess the effectiveness of implementation interventions.

STRENGTHS AND LIMITATIONS

- While previous reviews have evaluated implementation interventions, to our knowledge, this review is the first to examine interventions to improve HF care, and to identify contextual factors associated with implementation success.
- We conducted an extensive search of 9 databases and include 35 studies spanning 8 implementation intervention categories.
- A major limitation of our review is that a majority of the studies (N=26) used observational or quasi-experimental designs, which are subject to bias and confounding. Only 9 studies were RCTs.

INTRODUCTION

Heart Failure (HF) has a prevalence of approximately 10% in the elderly, and is a common cause of hospitalization and death in older adults.[1] Patients diagnosed with HF have a 30% risk of mortality at 3 years, and those hospitalized for HF face a substantially higher risk.[1] Evidence-informed HF treatments can improve clinical outcomes and recommendations surrounding their use are published in clinical practice guidelines. [2,3,4,5] Class I/Level A recommendations are supported by strong evidence, and are associated with reduced hospitalization and mortality; these include assessment of heart function, self-care education, pharmacotherapy, and device

therapies.[2] However, studies show that the uptake of these guidelines by physicians into routine clinical practice remains slow and inconsistent.[6,7,8]

Implementation interventions are designed to bridge the gap between evidence and practice, and are broadly classified at the provider, organizational, or health systems levels. Interventions may be single or multifaceted.[9] Implementation success also depends on the intervention-development process and organizational context. While previous reviews have evaluated implementation interventions,[10] none, to our knowledge, have evaluated interventions within HF care or identified contextual factors associated with implementation success.

Accordingly, the primary objective of our review was to examine the effectiveness of implementation interventions in increasing physician adherence to the specified HF guideline recommendations. Our secondary objectives were to assess the effect of implementation interventions on clinical outcomes, and to identify process and contextual factors that influence implementation success.

METHODS AND ANALYSIS

The systematic review protocol is registered in the International Prospective Register of Systematic Reviews (PROSPERO: CRD42015017155), and published in a peer-reviewed journal.[11] The only deviation from the protocol was the inclusion of uncontrolled before-after studies.

Eligibility criteria

We included trials evaluating 1 or more interventions aimed at improving physician adherence to Class I HF guidelines, relative to usual care. Interventions were categorized by level (i.e. provider-, organization-, systems- level) and type (i.e. education, decision-support, financial

incentives) according to the Cochrane Effective Practice and Organization of Care (EPOC) taxonomy.[9]

Outcomes

While implementation interventions were targeted towards healthcare providers, outcomes were measured at the level of the patient (e.g. number of patients receiving guideline-appropriate care). Primary outcomes were process indicators, defined as measures that assess guideline-consistent activities undertaken by a provider.[12] The primary outcomes included the proportion of eligible HF patients who: were prescribed a guideline-recommended pharmacological treatment such as β-blockers, angiotensin-converting-enzyme inhibitors (ACEIs), angiotensin II receptor blockers (ARBs), or mineralocorticoid receptor antagonists (MRAs); were referred for implantable cardioverter defibrillator (ICD) and/or cardiac resynchronization therapy (CRT) consideration; were provided self-care education at discharge; and/or had their left ventricular ejection fraction (LVEF) quantified. Secondary outcomes were clinical outcomes such as HF-related hospitalizations, readmissions and mortality. In the absence of HF-specific clinical outcomes, we extracted and reported all-cause clinical outcomes.

Study design

We included randomized controlled trials (RCTs), cohort studies (with comparisons), controlled and uncontrolled before and after studies, and interrupted time series studies.

Study selection

We searched for all English language articles published since 1990 in MEDLINE, EMBASE, HEALTHSTAR, CINAHL, The Cochrane Library, The Campbell Collaboration, The Joanna Briggs Institute Evidence Based Practice Database, The Agency for Healthcare Research and

Quality (AHRQ) Evidence-based Practice Centers' Research Reports, and the University of York Centre for Reviews and Dissemination Database. Our primary search strategy used the terms: heart failure, guideline adherence, practice guideline, evidence-based medicine, implement (Appendix 1). Our secondary search included terms for each of the different EPOC intervention types and heart failure (Appendix 2). Two authors independently screened titles and abstracts, and then assessed select full-text articles according to the eligibility criteria.

Data extraction and management

Two authors independently extracted details about study design, statistical analysis, intervention, patient and provider characteristics, follow-up, and outcomes using the EPOC Data Collection Checklist.[9] In addition, the Process Redesign framework was used to extract and synthesize details on the intervention-development process, and relevant contextual factors.[13]

Assessment of risk of bias

In addition to identifying the limitations inherent within specific study designs, two authors independently applied design-specific criteria to assess the internal validity of studies retained for analysis. We used the criteria outlined in the EPOC Data Collection Checklist to evaluate RCTs, cluster RCTs, controlled before-after studies, and interrupted time series studies.[9] For cluster RCTs, we used the additional criteria of recruitment bias, loss of cluster, and incorrect analysis according to the Cochrane Handbook of Systematic Reviews of Interventions.[14] For cohort studies, we utilized the Cochrane Collaboration's Tool to Assess Risk of Bias in Cohort Studies.[15] For uncontrolled before-after studies, we used the National Institute of Health's Quality Assessment Tool for Before-After Studies With No Control Group.[16] Because our goal was to assess internal validity, we did not use tool criteria pertaining to applicability or

external validity, precision, and quality of reporting. We categorized studies as low risk of bias if 1 criterion was not satisfied, medium risk if 2 to 3 criteria were not satisfied, and high risk if more than 3 criteria were not satisfied.

Data synthesis

We classified the implementation interventions according to the level targeted (provider, organization, and system) and the type of intervention (e.g. education, decision-support, audit-and-feedback, financial) using the EPOC Taxonomy.[9] An abbreviated version of the EPOC Taxonomy is presented in Table 1. We explored the suitability of a meta-analysis of the results within each intervention category by first assessing clinical heterogeneity at face value on the basis of included patient populations, settings (inpatient/outpatient), intervention types, and outcome measures. We then assessed statistical heterogeneity using the I^2 statistic, defining substantial heterogeneity as I^2>75%. For studies not suitable for meta-analysis, we narratively synthesized results.[17,18] We performed vote counting for each outcome measure in each EPOC intervention category, by noting the number of studies reporting significant improvements compared to those with no significant improvements.

Table 1. Effective Practice and Organization of Care Taxonomy

Intervention	Description
Provider Level	
Education	Distribution of educational materials; education sessions; or education outreach visits to providers
Audit and Feedback	Summary of clinical performance over a specified period with or without recommendations for clinical action. Information was obtained from medical records, computerized databases, or patients' observations
Reminders	Patient- or encounter- specific information provided verbally, on paper, or on a computer screen to prompt health professionals perform or avoid certain action
Organization Level	
Changes in medical	Modification of existing medical records systems (e.g. changing from

records systems	paper to computerized records)
Clinical multidisciplinary teams	A team of health professionals of different disciplines who work collaboratively to care for patients
Clinical pathways	Evidence-based care management tool for a specific group of patients with a predictable clinical course
Systems Level	
Provider financial incentives/penalties	Financial reward or penalty for specific action by an individual provider
Institutional financial incentives/penalties	Financial reward or penalty for specific action by an institution or group of providers

Contextual factors

Context generally refers to the physical, social, political, and economic influences on healthcare practices.[19] We used the Process Redesign framework to systematically evaluate contextual factors that may influence the effectiveness of implementation interventions.[13] The Process Redesign framework classifies context into categories: outer setting, inner setting, and characteristics of individuals and teams. The inner context refers to the structural characteristics of the clinical setting (e.g. inpatient, outpatient, community-based care, academic status), networks and communications, culture, and climate. The characteristics of individuals and teams more specifically refer to professional roles, responsibilities, and authority within the organization. The outer context refers to factors related to the broader social, political, and economic environment in which the intervention is applied. We considered processes that introduced and adapted the intervention to the organization as part of the intervention, rather than the context. An abbreviated and modified version of the framework is presented in Table 2.

Table 2. Adapted Process Redesign Framework

Construct	Description
Process of Implementation (applied here as an intervention factor)	

Planning	Degree to which intervention steps are developed in advance of implementation and with consideration of various possible scenarios
Assessing	Formal assessment of the problem or condition to be changed, including needs of users, and barriers and facilitators of change
Staging and iteration	Whether the implementation is carried out in incremental steps, refined iteratively, or implemented in its entirety within a specified period
Access to information, training, and education	Staff access to information or education about the intervention
Inner Setting (contextual factor)	
Team and network characteristics	Influence, breadth, depth, and role diversity of teams and networks engaged in the Process Redesign
Teams, networks, and communications	Quality of teams and social networks; formal/informal communication and information exchange within an organization or between organizations
Culture	Norms, values, and beliefs within a team, unit, or practice that affect views of process redesign and its implementation
Mandate	Whether adherence to the intervention is expected or mandated
Leadership commitment	Degree of commitment, involvement, and accountability of leaders and managers to quality improvement and to the specific intervention
Human factors	Whether features of the physical and technical environment of the practice are designed to optimize human use, accessibility, and uptake in patient care
Outer Setting (contextual factor)	
External networks	Degree to which an organization is networked with other organizations engaged in similar types of process redesign activities
External pressure	Pressure emanating from outside the organization to introduce an intervention
External policy and incentives/disincentives	Laws, regulations, governmental recommendations, and/or payment schemes that affect the decision to adopt or abandon the process redesign efforts
Characteristics of Individuals and Teams (contextual factor)	
Role	Individual's or team's role and responsibilities, and the extent of multiple or shared roles
Authority	Perceived and actual degree of authority to make decisions and act autonomously

RESULTS

Identification, screening, and selection of studies

Our systematic search produced 2424 unique articles, of which 2299 were excluded on the basis of title and/or abstract review. We assessed 126 full-text articles, of which 35 studies met eligibility criteria. We excluded articles that: were abstracts, protocols, or letters (N=9); did not test implementation interventions (N=20); did not focus on HF patients (N=3); had no comparator group (N=5); or had no outcomes of interest (N=54) (see Figure 1).

Fig 1. PRISMA flow diagram of study selection

Characteristics of included studies

Setting. A majority of the studies were conducted in the USA (N=25), and the remainder in Europe (N=9) and Australia (N=1). Sixteen studies were conducted in inpatient settings, 18 in outpatient settings, and 1 involved care in both settings (Table 3).

Table 3. Summary of studies evaluating strategies for the implementation of Heart Failure (HF) clinical guidelines

Author (year) Country	Setting	Study design	Unit of recruitment / analysis (N)	Intervention and Process of Implementation (when described)	Process outcomes *	Clinical outcomes *
Professional Interventions						
Education						
Thilly et al. (2003) France	Tertiary care; inpatient	Cluster RCT	Hospitals (20)/Patients (370)	**Intervention:** Cardiologists presented guidelines and discussed cases with colleagues. Educational aids and guideline booklets were supplied to physicians. **Process:** *Planning/Assessment* – Prior to developing the educational intervention, a preliminary survey was conducted to identify specific guideline deviations in practice. Guidelines determined to be of particular concern were made the focus of the intervention.	**Target ACEI +27%[a], p=0.003**	
Asch et al. (2005) USA	Tertiary care; inpatient	Controlled Before-after	Patients (489)	**Intervention:** Provider teams attended 3 training sessions where national Quality Improvement and HF experts guided them in studying, testing, and implementing systematic improvements in HF care processes.	**ACEI +18%[b], p<0.0001**; β-blockers -2%[b], P=0.49; LVEF +3%[b], p=0.49	
Audit and Feedback						
Kasje et al. (2006) Netherlands	Primary care	Cluster RCT	Providers (57)/Patients (508)	**Intervention:** Providers received patient-specific feedback on a sample of patients, and attended structured meetings to discuss guidelines and current management, identify problems, and propose solutions for improving patient care.	ACEI +5%[a], p>0.05	

				Process: *Planning/Assessment* – Optimal intervention design was determined through literature review. Specific barriers to guideline adherence were identified by physicians during peer-review meetings as part of the intervention.		
Frijling et al. (2003) Netherlands	Primary care	Cluster RCT	Practices (124)/Patients (236)	**Intervention:** Physician assistants provided physicians with a practice-specific feedback report, identified areas needing improvement, and provided guidance and resources for improvement.	Education odds ratio 0.85, p=0.636	
Cancian et al. (2013) Italy	Primary care	Before-after	Patients (1905)	**Intervention:** Performance data was aggregated across 21 health units. Project leaders reviewed data and identified barriers to unit leaders, who conveyed the data to all physicians involved. **Process:** *Access to information, training, education* – Intervention explained to participating physicians through two health unit training meetings.	**ACEI +3.6%[a], p=0.008; β-blockers +10.8%[a], p<0.0001**	
Matthews et al. (2007) USA	Tertiary care; outpatient	Before-after	Patients (265)	**Intervention:** Following discharge of patients from the hospital, outpatient physicians were provided quality-of-care reports outlining services received in hospital and areas for HF care improvement.	**ACEI +6.4%, p=0.042[a]**; β-blockers -1.1%[a], p=0.73; MRA +11.1%[a], p=0.26	
Reminders						
Ansari et al. (2003)	Primary care	RCT	Patients (115)	**Intervention:** Physicians received a list of their HF patients eligible for β-blockers as well as electronic	β-blockers -17%[a],	HF-related hospitalizat

USA				alerts when accessing patients' EMRs for first 2 visits after randomization. **Process:** *Planning/Assessment* – The intervention was designed to address a barrier identified at baseline.	p>0.05; Target β-blockers - 8%[a], p>0.05	ions +4%[a], p>0.05; 1-year all-cause mortality - 12%[a], p=0.05
Braun et al. (2011) Germany	Primary care	Before-after	Patients (190)	**Intervention:** Computer-based system displayed a pop-up window of a condensed version of the HF guidelines during clinical consultations.	ACEI - 4.4%[a], p=0.3; **β-blockers +12.3%[a], p=0.03**; **MRA +9.2%[a], p=0.04**	
Butler et al. (2006) USA	Tertiary care university hospital; inpatient	Before-After	Patients (1275)	**Intervention:** Computerized physician order entry system provided point-of-care reminders for select quality measures and included a prescription writer function. **Process:** *Planning/Assessment* – The intervention was developed iteratively prior to the intervention phase of the study. The program was modified based on institutional requirements, developer-initiated improvements, and user feedback.	ACEI +13%[a], p=0.10; **Education +53%[a], p<0.001**; LVEF +5%[a], p=0.86	
Qian et al. (2011) USA	Tertiary care university hospital; inpatient	Before-after	Patients (5000)	**Intervention:** Computer program flagged eligible patients not receiving ACEI/ARB. Pharmacists verified the flags and notified the medical team via EMR. Patients were re-flagged if no action was taken within 24 hours.	**ACEI +9.2%[a], p<0.002**	

				Process: *Planning* – Comprehensive Plan-Do-Study-Act cycle occurred over a period of 1 year prior to the intervention phase. Problems were identified in the system's operating process and adjusted to increase work-flow efficiency.		
Gravelin et al. (2011) USA	Cardiology clinics; outpatient	Before-after	Patients (6632)	**Intervention:** EMR screening tool identified patients with left ventricular ejection fraction <35% and prompted cardiologists to refer to electrophysiologist for consideration of Internal Cardioverter Defibrillator (ICD) and/or Cardiac Resynchronization Therapy (CRT).	**ICD/CRT referral: site 1 +47%[a], p<0.02**; **site 2 +40%[a], p<0.001**	
Organizational Interventions						
Changes in medical records systems						
Reingold et al. (2007) USA	Tertiary care university hospital; inpatient	Before-after	Patients (171)	**Intervention:** Existing HF order sets were modified to be more succinct and visually organized, with the addition of narrative information to encourage utilization. **Process:** *Planning/Assessment* – The improvement process was initiated 5 years in advance of intervention phase, and the intervention was developed based on staff feedback.	**ACEI +58%[a], p=0.008**	
Oujiri et al. (2011) USA	Tertiary care university hospital	Before-after	Patients (153)	**Intervention:** A discharge face sheet embedded into the EMR reminded physicians of evidence-based measures and required physicians to indicate reasons for unmet measures. **Process:** *Planning/Assessment* – The institution's admission and discharge processes were reviewed extensively to identify barriers to guideline-adherence at baseline, and these were addressed in the	**ACEI +18%[a], p<0.01**; Education +5%[a], p>0.05; LVEF +12%[a], p>0.05	

				intervention design.		
Baker et al. (2011) USA	Primary care	ITS	Patients (276)	**Intervention:** Pre-visit paper reminders of outstanding quality deficits were printed and placed outside the patient's examination room to supplement existing electronic reminders within the EMR. **Process:** *Planning/Assessment* – Following earlier introduction of an electronic reminder system, physician adherence to guideline recommendations was evaluated. Reasons for gaps were identified among a subset of physicians and addressed in the design of the paper intervention.	ACEI +0% per year[c], p=0.95; **β-blockers +2.9% per year[c], p=0.004**	
Persell et al. (2011) USA	Primary care	ITS	Patients (not clear)	**Intervention:** An existing reminder system was updated and standardized to increase user-friendliness at the point of care. **Process:** *Planning/Assessment* – Limitations in the EMR system were identified at baseline and addressed in the system re-design.	**ACEI +5.3% per year[c], p<0.001**; **β-blockers +5.7% per year[c], p<0.001**	
Clinical multidisciplinary team						
McCarren et al. (2013)	Tertiary care;	Cluster RCT	Hospitals (12)/Patients	**Intervention:** Pharmacists in both arms were asked to invent methods to improve prescribing practices.	**Target β-blockers**	

USA	outpatient		(220)	Intervention arm pharmacists also received a list of patients with suboptimal HF therapy. **Process:** *Planning* – Intervention methods were designed to be pragmatic (i.e. data collection and presentation required by each pharmacist was minimal to promote participation)	**odds ratio 1.9, p<0.05**	
Mejhert et al. (2004) Sweden	Tertiary university hospital; outpatient	RCT	Patients (208)	**Intervention:** A nurse monitored patients and adjusted their medications under the supervision of a senior cardiologist.	**Target ACEI +14%[a], p<0.05**; ACEI -5%[a], p>0.05; β-blockers -6%, p>0.05	4-year all-cause mortality +7%[a], p>0.05 4-year all-cause readmissions +0%[a], p>0.05
Kasper et al. (2002) USA	Tertiary university hospital; outpatient	RCT	Patients (200)	**Intervention:** In the intervention group, HF nurses closely followed up with patients post-discharge and implemented the cardiologist-developed treatment algorithm. The control group received care from the primary physician alone.	ACEI +12.3%, p=0.07; β-blockers +8.1%[a], p=0.27;	
Ansari et al. (2003) USA	Primary care at a university hospital; outpatient	RCT	Patients (105)	**Intervention:** With permission from the provider, NPs were responsible for initiating, titrating, and maintaining eligible HF patient on β-blockers. **Process:** *Planning/Assessment* – The intervention was designed to address a barrier identified at baseline.	**β-blockers +32%[a], p<0.001; Target β-blockers +33%[a], p<0.001**	HF-related hospitalizations -1%[a], p=0.66 1-year all-cause mortality -5%[a], p=0.05

Warden et al. (2014) USA	Tertiary care; inpatient	Before-after	Patients (150)	**Intervention:** Pharmacists reviewed patients' records, addressed prescription concerns to the primary care team, and made suggestions for medication treatment and monitoring.	**ACEI +13%[a], p=0.02**; **Education +17%[a], p=0.007**	30-day HF-related readmissions -12%[a], p=0.11 **30-day all-cause readmissions -21%[a], p=0.02**
Martinez et al. (2013) USA	HF clinic; outpatient	Before-after	Patients (144)	**Intervention:** Pharmacists managed a clinic in which they initiated and adjusted medication dosages based on clinical characteristics. **Process:** *Planning/Assessment* – The intervention was introduced to address previously identified gaps in HF care	**Target ACEI +21.9%[a], p=0.007**; **Target β-blockers +24.3%[a], p=0.012**	
Clinical pathways						
Panella et al. (2005) Italy	Tertiary care; inpatient	RCT	Patients (68)	**Intervention:** An integrated care pathway displayed patient care goals and provided the sequence and timing of actions necessary to achieve goals. **Process:** *Information, training, and education* – The intervention group received training to use the pathway *Planning/Assessment*: There was a 6-month planning period prior to the intervention phase to build work teams, review practices, develop the pathway, and perform ongoing evaluation and improvement.	ACEI +8.28%[a], p>0.05; **Education +27.7%[a], p<0.01**; **LVEF +35.4%[a], p<0.01**	30-day all-cause readmissions -4.36%[a], p>0.05 **30-day all-cause mortality -7.33%[a], p<0.05**
Garin et al.	Tertiary	Before-	Patients (363)	**Intervention:** A computerized clinical pathway	Target	30-day all-

(2012) Switzerland	care; inpatient	after		included order sets for each stage of the hospital stay and required specific evaluation, treatment, and education criteria to be met prior to the next stage.	ACEI +0.2%[a], p=0.97; **β-blockers +14.3%[a], p=0.006**; **LVEF +16%[a], p=0.002**	cause mortality -0.4%[a], p=0.8; 90-day all-cause mortality -0.8%[a], p=0.11 30-day all-cause readmissions -6.6%[a], p=0.11; 90-day all-cause readmissions -8.2%[a], p=0.11
McCue et al. (2009) USA	Tertiary care; inpatient	Before-after	Patients (6013)	**Intervention:** A clinical pathway comprised an order sheet, clinical outcomes monitoring checklist, explanations for nursing, and disease-specific patient education forms. **Process of implementation:** *Planning/Assessment* – Design of the clinical pathway was dynamic; practitioner feedback was continuously sought and incorporated into pathway design throughout the intervention period.	**ACEI +17.2%[a], p<0.001**; **LVEF +10.6%[a], p<0.001**	
Ranjan et al. (2003) USA	Tertiary care; inpatient	Before-after	Patients (371)	**Intervention:** A clinical pathway for HF care was implemented.	**ACEI +33%[a], p<0.001**	
Whellan et al.	HF	Before-	Patients (117)	**Intervention:** Based on predefined protocols and	**β-blockers**	**1.5**

(2001) USA	clinic; outpatient	after		severity of the patient's illness, a follow-up schedule for clinic visits and telephone calls was initiated at the time of enrolment. **Process:** *Access to information, training, and education* – Pre-enrollment, internal medicine house-staff and primary care physicians in the network were presented an outline of the program; pocket cards with inclusion criteria and referral phone numbers were also provided for all nursing stations at the hospital. *Planning/Assessment* – The program was designed by adapting practices from other disease management programs to the needs of the local health system.	**+24%[a], p<0.01**; **Target β-blockers +7%[a], p<0.01**; ACEI +1%[a], p=0.75	**(control) vs. 0 (intervention) all cause hospitalizations per patient-year, p<0.01**
Financial Interventions						
Provider incentives						
Esse et al. (2013) USA	Tertiary care; inpatient	Before-after	Patients (4304)	**Intervention:** Primary physicians responsible for patients in the Medicare Advantage Prescription Drug Plan were financially compensated for utilization of evidence-based HF therapy.	ACEI – 1.85%[a], p=0.244; β-blockers - 0.06%[a], p=0.972	All-cause hospitalizations: acute visits +2.58%[a], p=0.100; ER visits +0.62%[a], p=0.675
Institutional incentives						
Lindenauer et al. (2007) USA	Tertiary care; inpatient	Controlled Before-after	Patients (50678)	**Intervention:** Hospitals submitted data on 33 HF quality measures. Those performing in the top decile for a given year received a 2% bonus payment in addition to usual Medicare reimbursement.	ACEI +2%[b], p=0.34; **LVEF +5.1%[b], p<0.001**	

Sutton et al. (2012) England	Tertiary care; inpatient	Controlled Before-after	Patients (not clear)	**Intervention:** Hospitals submitted data on 28 HF quality measures. At the end of the first year, hospitals that reported quality scores in the top quartile received a 4% bonus.	ACEI +1.4%[b]; LVEF +8.1%[b]; no p-values reported Education +15.2%[b]	30-day all-cause mortality -0.6%[a], p=0.3
Combined Interventions						
Peters-Klimm et al. (2008) Germany	Primary care	Cluster RCT	Providers (37)/Patients (168)	**Intervention:** Physicians engaged in 4 didactic, interdisciplinary educational meetings with primary care physicians, cardiologists, and psychosomatic specialists; and received pharmacotherapy feedback (% target dose) on individual patients. **Process:** *Information, training, and education* – Physicians received initiation visit, which included an introduction to the intervention and a handout of the trial investigator file. *Opinion leaders* – Education component of the intervention was provided by a senior cardiologist with didactic expertise.	ACEI +8.7%[a], p=0.15; **Target ACEI +12.3%[a], p=0.04**; β-blockers -4.8%[a], p=0.67; Target β-blockers +1.7%[a], p=0.26	
Fonarow/Gheorghiade et al. (2010/2012) USA	Cardiology clinic; outpatient	Before-after	Patients (15 177)	**Intervention:** The intervention consisted of a guideline-based clinical decision support tool kit, educational materials, practice-specific data reports, benchmarked quality-of-care reports, and structured educational opportunities. **Process:** *Information, training, and education* – A 1-day workshop for practice personnel provided overview of study goals and tool kit. *Planning/Assessment* – A steering committee was	**ACEI +6.7%[a], p<0.001**; Target ACEI +1.8%, p=0.053[a]; **β-blockers +7.4%[a], p<0.001**;	

				appointed to follow a structured, rigorous, guideline-driven process to develop the pathways and tools prior to the intervention phase. *Opinion leaders* – The educational component of the intervention included expert opinions regarding best practices in HF care.	Target β-blockers +9.8%, p=<0.001; **MRA +27.4%[a], p<0.001**; Target MRA +4.1%, p=0.107; **Education +9.1%[a], p<0.001**; **ICD referral +30.3%[a], p<0.001**	
Goff et al. (2005) USA	Primary care	Before-after	Patients (3141)	**Intervention:** Physicians received performance audit and feedback, aggregated across a multicounty health service area; and patient-specific chart reminders regarding medications and education. **Process:** *Planning* – The intervention planning team identified and addressed barriers at provider and patient levels. *Patients* – The intervention planning team developed an educational brochure based on results of focus groups with HF patients.	ACEI - 2.7%[a], p=0.26; **β-blockers +15.2%[a], p<0.0001**; **LVEF +4.3%[a], p<0.0001**	

Riggio et al. (2009) USA	Tertiary care; inpatient	Before-after	Patients (4728)	**Intervention:** The intervention consisted of a computerized discharge checklist with electronic prompts on medication use, LVEF assessment, and discharge instructions; personalized resident performance reports; financial bonus for residents achieving a threshold of quality compliance; lectures on hospital/state/nation quality performance. **Process:** *Planning* – The intervention planning team received and incorporated ongoing feedback from residents and physicians in developing the reminder system prior to the intervention phase.	**ACEI +15.7%[a], p<0.001**; **Education +55.8%[a], p<0.001** LVEF -0.2%[a], P=0.78	
Scott et al. (2004) Australia	Mixed; Tertiary and primary care practices	Before-after	Patients (904)	**Intervention:** The in-hospital component consisted of: reminders on patient charts; clinical pathways for emergency chest pain assessment and management; educational presentations as grand rounds, seminars, workshops, and case-based meetings; briefing of hospital and primary care physicians by clinical pharmacists. The discharge-planning component consisted of standardized discharge referral summaries with personal treatment targets; medication lists forwarded to community pharmacists; pharmacist counselling of patients about lifestyle changes, drug therapy, and risk-factor modification; post-discharge telephone follow-up by clinical pharmacists of high-risk patients. **Process:** *Planning/Assessment* – Intervention was designed to address several implementation barriers that were identified through literature review.	**ACEI +15%[a], p=0.04; β-blockers +21%[a], p=0.01**; LVEF +9%[a], p=0.06	30-day HF-related readmissions +0.8%[a], p>0.05 **All cause mortality: 30-day -2.9%[a]; p<0.04, 6-month -7.6%[a], p<0.001**; **and 1-year all-cause mortality +10.4%[a], p=0.005**

Dykes et al. (2005) USA	Tertiary care; inpatient	Before-after	Patients (314)	**Intervention:** This involved a clinical pathway in EMR; a HF self-management education tool; and ongoing performance feedback.	Medication prescription +6.4%[a], p=0.389; **Education +64.9%[a], p=0.000**	

*Statistically significant results are shown in bold letters. [a]Absolute risk difference reported as (intervention group – control group). [b]Difference in difference (controlled before/after studies) reported as [intervention group (Time 2 – Time 1) – control group (Time 2 – Time 1)]. [c]Difference in rate of change (ITS studies) reported as (intervention group rate of change – control group rate of change). EMR, electronic medical record; NP, nurse practitioner; ACEI, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; MRA, mineralocorticoid receptor antagonist; LVEF, left ventricular ejection fraction.

Types of implementation interventions. Thirteen studies offered interventions directed at the level of healthcare providers, 15 at the organization level, 3 at the health system level, and 4 across multiple levels. Provider-level interventions included: audit and feedback (N=4 studies),[19-22] reminders (N=5),[24-28] education (N=2),[29,30] and a combination of these (N=2).[31,32] Organization-level interventions included: changes in medical records systems (i.e. adaptations to existing systems on the basis of organizational need) (N=4),[33,34,35,36] clinical multidisciplinary teams (N=6),[24,37-41] and clinical pathways (N=5).[42-46] System-level interventions included: financial incentives for providers (N=1) [47] and financial incentives for institutions (N=2).[48,49] Four studies offered interventions across multiple levels. A common feature across all 6 multifaceted interventions was the use of audit and feedback (Tables 3 and 4).

Table 4. Implementation strategies classified according to the EPOC Taxonomy

	Professional													Organizational														Financial			Multi-level			
	Thilly et al. (2003)	Asch et al. (2003)	Kasje et al. (2006)	Cancian et al. (2013)	Matthews et al. (2007)	Frijling et al. (2003)	Ansari et al. (2003)	Braun et al. (2011)	Butler et al. (2006)	Qian et al. (2011)	Gravelin et al. (2011)	Peters-Klimm et al. (2008)	Goff et al. (2005)	McCarren et al. (2003)	Mejhert et al. (2004)	Kasper et al. (2002)	Ansari et al. (2003)	Warden et al. (2014)	Martinez et al. (2013)	Panella et al. (2005)	Garin et al. (2012)	McCue et al. (2009)	Ranjan et al. (2005)	Whellan et al. (2001)	Reingold et al. (2007)	Oujiri et al. (2011)	Baker et al. (2011)	Persell et al. (2011)	Esse et al. (2013)	Lindenauer et al. (2007)	Sutton et al. (2012)	Fonarow/Gheorghiade et al. (2010/2013)	Riggio et al. (2009)	Scott et al. (2004)	Dykes et al. (2005)
Professional																																		
Education	x	x										x																				x		x	x
Local opinion leaders																																		
Audit and feedback			x	x	x	x						x	x																			x	x	x	x
Reminders							x	x	x	x	x		x																				x	x	
Organizational																																		
Clinical multidisciplinary teams														x	x	x	x	x	x																
Clinical pathways																				x	x	x	x	x								x		x	x

Changes in medical records systems	x	x	x	x					
Continuity of care									x
Financial									
Provider incentives/penalty					x			x	
Institutional incentives/penalty						x	x		

Study design. Among the 35 studies included, 9 were RCTs. Four were randomized at the level of patients,[24,37,38,42] and 5 were cluster randomized by practice or hospital.[20,21,29,31,39] Twenty-three studies used quasi-experimental designs: 3 were controlled before-after studies,[30,39,48] 2 were interrupted time series studies,[32,33] and 18 were uncontrolled before-after studies.[22,23,25-28,32-36,40,41,43,44,50,51] Three studies used a retrospective cohort design.[45-47] (see Table 3)

Risk of bias. Most studies were deemed to have medium risk of bias when assessed using design-specific criteria (Appendix 3). Four patient-level RCTs,[24,37,38,42] and 4 of the 5 cluster RCTs had low risk of bias.[21,29,31,42]

Quality of reporting. We evaluated the quality of reporting in RCTs using the CONSORT statement, including the extension for cluster RCTs. Among the 4 RCTs, 3 did not provide information on the methods of randomization or allocation concealment.[24,37,42] None of the 4 studies reported the precision of effect size estimates or provided relative effect sizes in addition to absolute risk differences.[24,37,38,42] Among the 5 cluster RCTs, 4 did not provide information on the methods of randomization or allocation concealment,[20,29,31,39] 3 did not describe eligibility criteria,[20,21,29] 3 did not provide sample size calculations,[20,31,39] and 4 did not provide intra-cluster correlation values.[20,21,29,39]

Outcomes reported. Thirty-four studies reported the proportion of patients prescribed recommended medications (i.e. ACEI/ARBs, β-blockers, MRAs); 28 studies reported prescription of indicated medications at any dose,[20,22-24,26,27,31-38,40,42-49,52-54] and 9 reported prescriptions of medications at target doses.[24,29,31,37,39,41,43,44,51] Other studies reported: patient self-care education prior to discharge (N=9);[21,25,36,40,42,49,50,52,54] referrals for ICD/CRT (N=2),[28,50] and LVEF assessments

(N=11).[25,30,32,36,42,43,45,48,49,52,53] In addition to these primary outcomes, 11 studies reported clinical outcomes such as mortality, hospitalization, and readmission rates.[24,30,37,38,40,42,43,44,47,49,53] I^2 calculations produced a value greater than 80% for most categories of interventions, precluding the possibility of a meta-analysis. Therefore, the studies were synthesized narratively.

Effectiveness of Implementation Interventions

A summary of study outcomes is presented in Table 3. A majority of studies (n=29, 83%) reported significant improvements in at least one primary outcome.

Prescription of indicated medications. Reminders, clinical pathways, changes in medical records systems, and multifaceted interventions were commonly associated with an increase in guideline-recommended prescriptions. In 4 studies that reported prescriptions of more than 1 indicated medication, significant improvements were observed in the prescription of β-blockers and MRAs, but not in the prescription of ACEIs. In these studies, the prescription rates at baseline for ACEIs were substantially higher than those of β-blockers or MRAs, ranging from 78.0% to 86.3%.[26,32,34,44]

Reminders. Two of 4 studies on reminders within electronic medical records (EMRs) reported a significant increase in the percent of patients prescribed an indicated medication.[26,27] One study in which reminders were unsuccessful had suboptimal intervention fidelity; stratification by actual use of the reminder system revealed a significant improvement in prescription rates.[25]

Clinical pathways. Four of 5 studies on clinical pathways reported a significant increase in the percent of patients prescribed an indicated medication.[43-46] The single study that reported no

significant change was an RCT in a remote community hospital, in contrast with the urban and/or teaching hospital settings of other clinical pathway studies.

Medical records systems. All four studies evaluating changes to EMRs reported significant increases in the percent of patients prescribed an indicated medication.[33-36] In each of these interventions, existing EMRs were enhanced by addressing identified limitations (Table 3).

Combination interventions. Two studies evaluated combinations of provider-level interventions. A combination of education with audit and feedback did not significantly increase the percent of patients prescribed an indicated medication,[31] while a combination of education, reminders, and audit and feedback did.[32]

Four studies combined implementation interventions across different levels of the EPOC taxonomy.[50-54] Two studies combined clinical pathways with audit and feedback; 1 reported a significant increase in the percent of patients prescribed an indicated medication.[50] Another study that combined a computerized order set, reminders, audit and feedback, financial incentives, and provider educational meetings, also reported a significant increase in the percent prescribed an indicated medication. [52] Finally, an intervention that fostered hospital-community integration using a combination of reminders, education for providers, audit and feedback, discharge summaries, and patient follow-up by pharmacists [53] reported a significant increase in β-blocker prescriptions in-hospital, and in all medications 6-months post-discharge.

Prescription of target-dose medications. Clinical multidisciplinary team interventions were consistently successful in increasing prescription of target-dose medications, with 3 of 4 studies reporting significant improvements for this outcome.[24,37,41] The 3 successful clinical multidisciplinary team interventions - including 2 RCTs [24,37] - involved nurses or pharmacists initiating or titrating medications according to a protocol. In contrast, an unsuccessful

intervention tasked pharmacists with improving prescribing practices, without clearly defining the mechanism to do so.[39]

One of 2 studies [43,44] evaluating clinical pathways reported significant increases in target dose prescription.[44] Of the two studies evaluating multifaceted interventions, an intervention combining education with audit and feedback reported significant improvements in target dose prescription,[31] while a comprehensive intervention combining education, reminders, audit and feedback, and clinical pathways did not.[51] In the successful multifaceted intervention, feedback was focused strictly on medication dosing for individual patients.[31]

Provision of patient self-care education. Only 9 studies reported on the provision of self-care education. Three multifaceted intervention studies reported this outcome measure, with a significant improvement in each case.[50,52,54] Provision of patient education also increased with a reminder system,[25] a clinical multidisciplinary team,[40] and a clinical pathway.[42] In contrast, interventions that did not produce significant improvements included: audit and feedback,[21] and changes to medical records systems.[36] One study, on financial incentives, did not report statistical significance.

LVEF assessment. Eleven studies reported the percent of patients who received an LVEF assessment. All three clinical pathway studies, including an RCT, reported significant improvements in this outcome.[42,43,45] Of the 2 studies evaluating institutional financial incentives [48,49], only 1 reported significant improvements.[48] Only 1 of 3 studies [32,52,53] evaluating multifaceted interventions that included audit and feedback as well as reminders reported significant increases in LVEF assessment.[32] Education,[30] reminders,[25] and changes in medical records systems,[36] did not significantly increase LVEF assessment

ICD/CRT referral. Only 2 studies measured the percent of indicated patients who received an ICD/CRT referral. These studies evaluated a reminder intervention,[28] and a multifaceted intervention combining reminders, clinical pathways, education, and audit and feedback,[50] respectively, with significant improvements reported in each case.

Evidence from RCTs

Very few RCTs were available for most intervention types; none were available for medical records system changes or financial incentives. Four RCTs evaluated the effect of clinical multidisciplinary teams on overall prescription rates,[24,37,38] and target-dose prescriptions.[24,37,39] Among these, 1 of 3 reported significant improvement in overall prescription rates,[24] and 2 of 3 reported significant improvements in target-dose prescriptions.[24,37] Two RCTs evaluated audit and feedback interventions,[20,21] with no significant improvements in the reported outcomes. An RCT evaluating education [29] reported significant improvements for all outcomes measured, while am RCT assessing reminders [24] reported no significant improvements. The RCT evaluating a clinical pathway [42] significantly increased patient self-care education,[42] and the RCT assessing a multifaceted intervention significantly increased the prescription of some target-dose medications.[31]

Clinical outcomes

While 5 of the 6 studies reporting all-cause mortality successfully improved process outcomes, only 2 reported a significant decrease in mortality: an RCT evaluating a clinical pathway [42] and a before-after study assessing a multifaceted transitional care intervention.[53]

While all 6 studies reporting all-cause hospitalization or readmission rates improved process outcomes [30,37,40,43,43,44], significant improvements in the clinical outcomes were only

reported in 2: a multidisciplinary team study [40] and a clinical pathway study.[44] Both studies used a before-after design with medium risk of bias. There was no improvement in 2 studies assessing clinical pathways [42,43], 1 assessing multidisciplinary interventions [37], and 1 assessing an educational intervention [30].

While 3 of 4 studies reporting HF-related hospitalizations or readmissions [12,32] improved process outcomes, none reported significant improvements in the HF-related clinical outcomes.

Process of implementation (Table 3)

Six studies reported provision of preliminary training, education, and resources to introduce clinicians to the implementation intervention and encourage utilization; in each case interventions were effective in improving at least 1 process outcome.[21,25,38,43,44] Eight studies assessed barriers to guideline implementation at baseline and adapted the interventions accordingly.[16,28,31,35,40,42,52] This was associated with implementation success for all interventions, with the exception of audit and feedback.[42] Six studies used an iterative process, whereby the program was regularly updated on the basis of institutional requirements and user feedback.[26,32,34,38,51,54] An iterative intervention-development process was associated with implementation success across the range of interventions in which it was reported.

Contextual factors (Appendix 4)

Inner setting. Five interventions that improved at least 1 process outcome reported leadership support from either the department or hospital-level.[26,32,39,51,52]

Outer setting. In 9 US studies,[26-28,34-36,40,51,54] there were preexisting initiatives by the Centers for Medicare and Medicaid Services (CMS) or The Joint Commission (TJC), including financial reimbursements or accreditation on the basis of HF readmission rates, and public

reporting of quality of care data. These contextual factors encouraged organizations to implement interventions to improve guideline adherence. This is in contrast to the lack of success observed when financial interventions were used as the implementation intervention itself.

DISCUSSION

In this systematic review, we assessed the effectiveness of implementation interventions aimed at improving physician adherence to Class I HF guideline recommendations. We synthesized our findings narratively as the variation in study design, intervention, and outcomes across studies precluded meta-analysis. We temper our discussion in accordance with the limitations of a narrative synthesis, to provide an overview of the current literature.

We found that a majority (83%) of 35 studies reported significant improvements in at least 1 process outcome. A process outcome commonly reported across studies and interventions was the proportion of patients prescribed an indicated medication. Electronic medical system interventions were associated with significant improvements in this outcome in 100% of studies (4/4 studies), followed by clinical pathways (80%, 4 of 5 studies), multifaceted interventions (66%, 4/6 studies), and reminders (50%, 2/4 studies). Very few studies on education or audit and feedback reported this outcome, making direct comparisons with other interventions challenging. However, on the whole, the results across a number of studies suggest that educational seminars,[30] and audit and feedback,[20,21] are ineffective in isolation, though they may be a supportive component of multifaceted interventions.[32,50,52,53]

Where 2 or more RCTs were conducted on a given implementation intervention, the results reinforced overall findings that: clinical multidisciplinary teams, with clear pre-defined

responsibilities, seem to be especially effective in titrating patients to their target dose;[24,37,38,39] and audit and feedback, in isolation, is largely ineffective.[20,21]

Improvements in process outcomes were rarely accompanied by improvements in clinical outcomes. One reason for this gap may be that interventions focusing exclusively on improving HF care may be insufficient to decrease all-cause mortality and readmissions in a patient population characterized by multiple comorbidities.[55,56] Furthermore, studies may not have had sufficient statistical power to demonstrate an improvement in clinical outcomes [11,23,31] The gap between process and clinical outcomes may also be explained by study designs that did not account for background trends or adjust for confounding variables. Finally, it is important to note that improvements in HF clinical outcomes are multifactorial and depend not only on the physician prescribing appropriate medications, but also on the patient's adherence to these medications, as well as follow-up care by other providers.[30] The studies that showed a trend toward reduction in HF-related readmissions, albeit not significant, are those that addressed more than 1 of these factors.[38,40]

Beyond the features of an implementation intervention, the process of its introduction and adaptation to the local setting is critical to its uptake and effectiveness. In particular, a planning period that assesses barriers at baseline and tailors the intervention based on provider feedback, along with comprehensive staff training on the use of the intervention appears to facilitate successful implementation.[14] Contextual factors are known to modify the effects of implementation efforts.[57,58] Based on the limited details available in the included studies, it appears that support and involvement of organization leaders, mandated utilization of the intervention, and external policies and incentives for guideline adherence seem to be associated with guideline uptake. Similarly, a 2011 study using iterative, formal discussions with a panel of

leaders in patient safety, healthcare systems, and methods, identified four context domains important to quality improvement initiatives, including teamwork and leadership involvement, and external factors (e.g. financial or performance incentives or patient safety regulations).[59]

Our findings are consistent with those of related reviews. For example, a review focusing on audit and feedback interventions found that they are largely ineffective unless providers also receive explicit instructions for improvement.[60] Furthermore, our results did not demonstrate a clear relationship between number of intervention components and intervention success. The existing evidence on the effectiveness of multifaceted interventions also tends to be mixed.[61,62] An extensive review by Grimshaw et al. concluded that while multifaceted interventions are not inherently more effective than single interventions, they may be more effective when built upon a comprehensive assessment of barriers.[63-65] Among the studies on multifaceted interventions, the 4 studies that reported significant improvements in medication prescription rates carefully considered barriers at baseline and sought user feedback throughout the intervention development process.[32,50-53]

These results also support recently published findings from the American Heart Association's comprehensive Get With The Guidelines (GWTG)-HF program. The program used a combination of educational approaches (e.g. organizational stakeholder and opinion leader meetings, collaborative learning sessions, and clinical champions), multidisciplinary teams, and public hospital performance reporting.[66] The intervention was also carefully adapted and introduced at each hospital site through collaborative discussions of barriers and solutions, and iterative plan-do-study-act (PDSA) cycles prior to the intervention phase.[67] The results demonstrate significant and comparable improvements over time in both teaching and non-teaching hospitals.

There were a number of limitations to our review. First, the variation in interventions, settings, study designs, and outcome measures precluded meta-analyses, and in turn, our ability to draw substantive conclusions regarding specific implementation strategies and their comparative effectiveness. We chose to use a "vote counting" approach to synthesis. While this method is useful in presenting an initial description of the trends found across studies, it is limited by the fact that it assigns equal weight to studies of varying sample sizes, effect sizes, and significance levels.[68]

Another limitation was the methodological quality of the primary studies. Most studies used observational and quasi-experimental study designs. Quasi-experimental and observational designs possess some inherent risks of bias. In uncontrolled before-after studies, which formed the majority of studies in this review, temporal trends or sudden changes make it difficult to attribute the observed effects to the intervention alone. A time-series design increases confidence with which the observed effect can be attributed to the intervention; however, it does not protect against simultaneous events that may influence the intervention effect. Controlled before-after studies can protect against these effects, but cannot match groups on the basis of unknown confounders. We found that most quasi-experimental and observational studies possessed at least a medium risk of bias. Though almost all included RCTs demonstrated low risk of bias, they were largely applied in the evaluation of multidisciplinary team interventions, and less so to the evaluation of other implementation interventions.

A minority of studies in this review (9 of 35 studies) were RCTs, considered the gold standard in establishing a causal link between an intervention and its outcome. Indeed, RCTs are an uncommonly used methodology in implementation studies. In a recent systematic review of implementation interventions for the management of ICU delirium, only 1 of the 21 studies was

an RCT, 16 were before-after studies, and the remaining were cohort studies.[69] In another review on implementation interventions to improve the use of pain management assessments for hospitalized patients, only 3 of the 23 studies were controlled clinical trials, and the remaining 20 were uncontrolled before-after or time-series studies.[70] While randomized trials are robust in methodology, they pose a number of logistical challenges that may make them suboptimal for implementation research; they are expensive and time consuming, often requiring years to complete.[71] Changes in health care delivery are often implemented under internal and external pressures that seek to resolve an institutional problem in the shortest time possible. Under such circumstances, quasi-experimental designs are often felt to be most feasible.[71,72] A solution may be found in pragmatic clinical trials – such as the stepped wedge cluster RCT - which can offer the methodological benefits of randomization while being sensitive to the challenges of implementation research.[73]

Another limitation was that many studies failed to provide adequate details on the intervention, context, barriers, facilitators, or fidelity to the intervention. A review by Proctor et al. explores the reporting challenges in implementation research in significant detail. It offers a theoretical discussion of principles for naming, defining, and specifying implementation interventions.[74]

Suggestions for future studies

We identify a number of ways in which future research on the effectiveness of implementation interventions may be strengthened. First, there is a need for implementation interventions to be evaluated using more robust study designs that also account for the pragmatic challenges of implementation research. Furthermore, reporting of studies should adhere to standardized guidelines in order to better facilitate comparison between interventions. An example of reporting guidelines is the Quality Improvement Minimum Quality Criteria Set (QI-MQCS),

which spans the spectrum of intervention characteristics and contextual factors.[75]. Implementation research in HF may also benefit from more careful consideration of the contextual factors that influence implementation success. Finally, in addition to examining process outcomes, the direct impact of implementation interventions on clinical outcomes should be examined more consistently.

CONCLUSIONS

In this review, the heterogeneity of interventions, study designs, and outcomes limited our ability to draw substantive conclusions regarding the comparative effectiveness of implementation interventions. Trends observed across the included studies suggest that effective implementation interventions include electronic medical records systems, clinical multidisciplinary teams, clinical pathways, and multifaceted interventions that include audit-and-feedback. There is a need for higher quality research to assess the effectiveness of implementation interventions on HF care processes and on clinical outcomes, and for the use standardized reporting guidelines. Future work in the area should also include a closer examination of the organizational and external implementation context in order to better facilitate targeted application of implementation strategies.

Contributors: HGCV, IDG, KH, and SC conceived the study, and all authors contributed to the study design. DS contributed to the search strategy, extracted and synthesized study data, and drafted and edited the manuscript. IDG, KH, RBH, and SC contributed intellectual input and edited the manuscript for critical content. IG contributed to the search strategy and extracted study data. HGCV informed the search strategy, synthesized study data, drafted and edited the manuscript, and obtained funding.

Acknowledgements: We would like to thank Mr. Quazi Ibrahim for his help with the statistical analyses.

Funding: This study was funded by Ontario's Ministry of Health and Long Term Care (MOHLTC) Health System Research Fund and Canadian Institutes of Health Research. HGCV receives research salary support from the MOHLTC and Hamilton Health Sciences Career Research Award.

Competing interests: We have read and understood BMJ policy on declaration of interests and declare that we have no competing interests.

Data Sharing Statement: All relevant study data can be found in the supplemental files.

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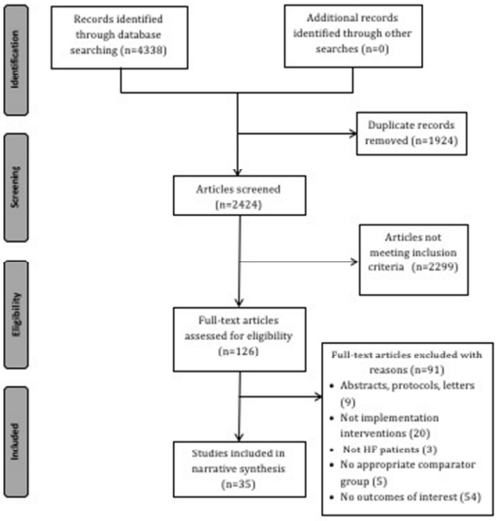

Fig 1. PRISMA flow diagram of study selection

338x190mm (54 x 54 DPI)

MEDLINE search strategy

1. exp Heart Failure/ or heart failure*.mp.
2. Guideline Adherence/ or guideline adherence*.mp.
3. practice guideline/ or practice guideline*.mp.
4. exp Evidence-Based Medicine/ or evidence based medicine*.mp. or evidence based practice*.mp.
5. implement*.mp. or standards.fs.
6. best practice*.mp
7. 1 and (2 or (5 and (3 or 4 or 6)))
8. limit 7 to (english language and yr="1990 -Current")

MEDLINE and EMBASE secondary search strategy

1. exp Heart Failure/
2. exp Cardiac Output, Low/
3. pay for performance.mp. or exp Reimbursement, Incentive/
4. clinical pathways.mp. or exp Critical Pathways/
5. clinical decision support system.mp. or exp Decision Support Systems, Clinical/
6. multidisciplinary team.mp.
7. Education, Medical, Continuing/ or educational interventions.mp.
8. (audit and feedback).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
9. Reminder Systems/ or reminders.mp.
10. 3 or 4 or 5 or 6 or 7 or 8 or 9
11. 1 or 2
12. 10 and 11
13. limit 12 to (english language and yr="1990 -Current")

Supplementary Table 1. Risk of bias among the RCTs and controlled before-after studies using the EPOC framework

Name, year	allocation concealment	Follow up of professionals	Follow up of patients	Blinded assessment of primary data	Base line measurement	Reliable primary outcome	Protection against contamination	Appropriate analysis	No Recruitment bias	No Loss of cluster	report of characteristics (2nd control site)
Cluster RCT											
Frijling et al. (2003)	+	+	+	-	+	-	+	+	+	+	N/A
Kasje et al (2006)	+	+	+	+	+	+	+	+	+	+	N/A
Klimm et al.(2008)	+	+	+	+	+	+	+	+	+	+	N/A
McCarren et al.(2013)	+	+	+	+	+	+	+	+	+	+	N/A
Thilly et al.(2003)	+	+	+	+	+	+	+	+	+	+	N/A
RCT											
Ansari et al. (2003)	+	+	+	+	+	+	+	N/A	N/A	N/A	N/A
Kasper et al.(2002)	+	+	+	+	+	+	+	N/A	N/A	N/A	N/A
Mejhert et al. (2004)	+	?	+	+	+	+	+	N/A	N/A	N/A	N/A
Panella et al. (2005)	?	+	+	+	+	+	+	N/A	N/A	N/A	N/A
Controlled Before-After											
Asch et al. (2005)	N/A	?	?	+	+	+	?	N/A	N/A	N/A	+
Lindenauer et al. (2007)	N/A	?	?	+	+	+	?	N/A	N/A	N/A	?
Sutton et al. (2012)	N/A	?	?	?	+	+	N/A	N/A	N/A	N/A	+

+, criteria met; -, criteria not met; ?, unclear; N/A, not applicable

Supplementary Table 2. Risk of bias among the interrupted time series using the EPOC framework

Name, year	protection against secular changes	Appropriate data analysis	Reason for the number of points pre and post	Shape of intervention effect specified	Protection against detection bias	Blinded assessment of primary outcome	Completeness of data set	Reliable primary outcome measure
Persell et al. (2011)	+	+	?	?	+	+	?	?
Baker et al. (2011)	+	+	?	?	+	+	+	+

+, criteria met; -, criteria not met; ?, unclear; N/A, not applicable

Supplementary Table 3. Risk of bias among the cohort studies using the Cochrane Collaboration framework

Name, year	Exposed/non-exposed from same group	Assessment exposure	Outcome of interest not present at study start	Matched for all prognostic variables or statistical adjustment	Assessment of presence/absence of prognostic factors	Assessment of outcome	Adequate follow up of cohorts	Similar co-interventions between groups
McCue et al. (2009)	+	+	+	?	?	+	+	?
Ranjan et al. (2003)	+	+	+	-	+	?	+	?
Esse et al. (2013)	+	+	+	+	+	+	+	?

+, criteria met; -, criteria not met; ?, unclear; N/A, not applicable

Supplementary Table 4. Risk of bias among the uncontrolled before-after studies using the National Institute of Health framework

Name, year	Eligibility criteria prior to defined enrollment	Outcomes clear, valid, reliable	Blinding of outcome assessors	Follow up of providers (80%)	Follow up of patients (80%)	Statistical analysis	Multiple outcome assessors
Cancian et al. (2013)	+	+	+	+	+	+	N/A
Matthews et al. (2007)	+	+	+	?	+	+	N/A
Braun et al. (2011)	+	+	+	+	+	+	N/A
Butler	+	+	+	?	?	+	N/A
Qian et al. (2011)	+	+	+	?	?	+	N/A
Gravelin et al. (2011)	+	+	+	+	+	+	N/A
Reingold et al. (2007)	+	+	+	?	?	+	N/A
Oujiri et al. (2011)	+	+	+	?	?	+	N/A
Warden et al. (2014)	+	+	+	?	?	+	N/A
Martinez et al. (2013)	+	+	+	?	?	+	N/A
Garin et al. (2012)	+	+	+	+	+	+	N/A
Whellan et al. (2001)	+	+	+	?	?	+	N/A
Fonarow et al. (2010)	+	+	+	?	?	+	N/A
Ghioghiarde et al. (2012)	+	+	+	?	?	+	N/A

Goff et al. (2005)	+	+	+	+	+	+	N/A
Riggio et al. (2009)	+	+	+	?	?	+	N/A
Scott et al. (2004)	+	+	+	?	?	+	N/A
Dykes et al. (2005)	+	+	+	?	?	+	N/A

+, criteria met; -, criteria not met; ?, unclear; N/A, not applicable

S5 Table: Contextual factors influencing implementation interventions among the included studies.

Study author, year	Contextual factors
Professional interventions	
Education	
Asch et al., 2005	Inner setting • *Leadership commitment*: Participating organizations demonstrated leadership commitment through a $125,000 contribution • *Mandate*: Intervention use was not mandated; following the training session, each organization was free to apply any implementation intervention they saw fit
Audit and Feedback	
Kasje et al., 2006	Inner setting • *Culture*: Most physicians were motivated to improve ACEI prescription • *Human factors*: Educational intervention was integrated into regular work flow Characteristics of individuals and teams • *Authority*: Primary care physicians were hesitant to change treatment initiated by a cardiologist
Cancian et al., 2013	Characteristics of individuals and teams • *Roles*: Limited primary care nurses; physicians dealt with most HF patients independently
Reminders	
Braun et al., 2006	Inner setting: • *Teams, networks, and communications*: In practices following the medical care centre model, primary care physicians and specialists shared the same equipment and rooms which promoted collaboration • *Culture*: Decision-making was considered a collaborative process
Butler et al., 2006	Outer setting: • *External policy and incentives/disincentives*: CMS was in the process of initiating public reporting of quality of care data Inner setting: • *Culture*: The research team was unable to effect cultural change to promote widespread adoption of the tool • *Mandate*: Intervention use remained optional (not mandated) during the intervention phase • *Human factors*: Intervention was designed to be unobtrusive

Qian et al., 2011	Outer setting: • *External policy and incentives/disincentives*: Reporting HF guideline-adherence data to TJC and CMS was mandatory Inner setting: • *Leadership commitment*: Leaders were involved in intervention planning
Gravelin et al., 2011	Outer setting: • *External policy and incentives/disincentives*: CMS reimbursed hospitals and physicians for appropriate ICD implantations
Professional interventions	
Changes in medical records systems	
Reingold et al., 2007	Outer setting: • *External policy and incentives/disincentives*: Implementation of computerized physician order-entry system was cited as a high national priority Inner setting: • *Culture*: Staff were committed to improving HF patient care • *Leadership commitment*: Emergency Department and Quality Improvement chairs released memos to encourage intervention use • *Measurement and data availability*: The team collected data on utilization of the intervention throughout the redesign process
Oujiri et al., 2011	Outer setting: • *External policy and incentives/disincentives*: TJC published performance measures for inpatient heart failure care Inner setting: • *Mandate*: Use of the implementation intervention was mandated for all hospital discharges • *Culture*: The intervention was well-received throughout the institution
Persell et al.,2011	Inner setting: • *Culture*: Staff were motivated to improve HF care
Clinical multidisciplinary teams	
Mejhert et al., 2004	Characteristics of individuals and teams • *Authority*: Nurses in program were allowed to institute and change the doses of medications
Kasper et al., 2002	NR
Martinez et	Outer setting:

al., 2013	• *External policy and incentives/disincentives*: CMS reduced reimbursement rates for hospitals with excessive HF readmissions
Clinical pathways	
McCue et al., 2009	Outer setting: • *External policies and initiatives*: TJC published performance measure for heart failure care
Financial interventions	
Provider incentives	
Esse et al., 2013	Outer setting: • *External policies and incentives*: The intervention was initiated by Medicare Advantage Prescription Drug Plan
Institutional incentives	
Lindenauer et al., 2007	Outer setting: • *External policies and incentives*: The intervention was developed collaboratively by the American Hospital Association, Federation of American Hospitals, and Association of American Medical Colleges.
Combined interventions	
Fonarow et al., 2010 Gheorghiadem et al., 2012	Inner setting: • *Mandate*: The use of provided resources was encouraged but not mandated; clinics were free to adopt/modify tools to their discretion
Goff et al., 2005	Outer setting: • *External policies and incentives*: State-wide quality improvement project with external funding to implement and evaluate the program
Riggio et al., 2009	Inner Setting: • *Leadership commitment*: Clinical Effectiveness Team that worked on developing the implementation intervention was chartered by the hospital's CEO and CMO Outer setting: • *External policies and incentives*: The Hospital Quality Initiative, launched by the US Department of Health and CMS, encouraged hospitals to report compliance with standardized performance measures. Better-performing hospitals were financially rewarded while poor performers were penalized. Hospitals in the study were at particular risk of financial penalty for non-compliance.
Scott et al., 2004	Inner setting: • *Leadership commitment*: Senior executives of state public health body were involved in the 2 year planning period preceding the intervention phase

	• *Culture*: Staff were motivated to improve HF

CMS, Centre for Medicare and Medicaid Services; TJC, The Joint Commission; CEO, chief executive officer; CMO, chief medical officer

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3-4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	4
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	4
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	4-5
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	5-6
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	S1 Appendix, S2 Appendix
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	5-6
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	6
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	6
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	6-7
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	N/A

PRISMA 2009 Checklist

Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	7

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	N/A
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	N/A
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	10-11
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	12-25 (Table 3)
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	Supp. Tables S3-S7
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	12-25 (Table 3)
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	30-35 (narr. synth)
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	N/A
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	N/A
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	36-38
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	38-40
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	40-41
FUNDING			

PRISMA 2009 Checklist

Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	submission form

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

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BMJ Open

Effectiveness of implementation interventions in improving physician adherence to guideline recommendations in heart failure: a systematic review

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2017-017765.R1
Article Type:	Research
Date Submitted by the Author:	05-Dec-2017
Complete List of Authors:	Shanbhag, Deepti; McMaster University, Bachelor of Health Sciences (Honours) Program Graham, Ian; Ottawa Hospital Research Institute, Clinical Epidemiology Program; University of Ottawa, Department of Clinical Epidemiology Harlos, Karen; University of Winnipeg, Department of Business and Administration Haynes, R. Brian; McMaster University, Department of Health Research Methods, Evidence, and Impact Gabizon, Itzhak; Population Health Research Institute, Population Health Research Institute; McMaster University, Department of Medicine Connolly, Stuart; Population Health Research Institute; McMaster University, Department of Medicine Van Spall, Harriette Gillian Christine; Population Health Research Institute, Knowledge Translation Program and CVD Risk Factors Program - Heart Failure; McMaster University, Department of Medicine
Primary Subject Heading:	Health services research
Secondary Subject Heading:	Evidence based practice, Cardiovascular medicine
Keywords:	Heart failure < CARDIOLOGY, Change management < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Quality in health care < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Protocols & guidelines < HEALTH SERVICES ADMINISTRATION & MANAGEMENT

Effectiveness of implementation interventions in improving physician adherence to guideline recommendations in heart failure: a systematic review

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Keywords: heart failure, healthcare quality, change management, clinical guidelines, implementation science, knowledge translation

Word Count: 4307

ABSTRACT

Background: The uptake of guideline recommendations that improve heart failure (HF) outcomes remains suboptimal. We reviewed implementation interventions that improve physician adherence to these recommendations, and identified contextual factors associated with implementation success.

Methods: We searched databases from January 1990 - November 2017 for studies testing interventions to improve uptake of Class I HF guidelines. We used the EPOC and Process Redesign frameworks for data extraction. Primary outcomes included: proportion of eligible patients offered guideline-recommended pharmacotherapy, self-care education, left ventricular function assessment, and/or intracardiac devices. We reported clinical outcomes when available.

Results: We included 38 studies. Provider-level interventions (N=13 studies) included audit and feedback, reminders, and education. Organization-level interventions (N=18) included medical records systems changes, multidisciplinary teams, clinical pathways, and continuity of care. System-level interventions (N=3) included provider/institutional incentives. Four studies assessed multi-level interventions. We could not perform meta-analyses due to statistical/conceptual heterogeneity. Thirty-two studies reported significant improvements in at least 1 primary outcome. Clinical pathways, multidisciplinary teams, and multifaceted interventions were most consistently successful in increasing physician uptake of guidelines. Among RCTs (N=10), pharmacist and nurse-led interventions improved target dose prescriptions. Eleven studies reported clinical outcomes; significant improvements were reported in 3, including a clinical pathway, a multidisciplinary team, and a multifaceted intervention. Baseline assessment of barriers, staff training, iterative intervention development, leadership commitment, and policy/financial incentives were associated with intervention effectiveness. Most studies (N=20) had medium risk of bias; 9 RCTs had low risk of bias.

Conclusion: Our study is limited by the quality and heterogeneity of the primary studies. Clinical pathways, multidisciplinary teams, and multifaceted interventions appear to be most consistent in increasing guideline uptake. However, improvements in process outcomes were rarely accompanied by improvements in clinical outcomes. Our work highlights the need for

improved research methodology to reliably assess the effectiveness of implementation interventions.

STRENGTHS AND LIMITATIONS

- While previous reviews have evaluated implementation interventions, to our knowledge, this review is the first to examine interventions to improve HF care, and to identify contextual factors associated with implementation success.
- We conducted an extensive search of 9 databases and include 38 studies spanning 9 implementation intervention categories.
- A major limitation of our review is that a majority of the studies (N=28) used observational or quasi-experimental designs, which are subject to bias and confounding. Only 10 studies were RCTs.

INTRODUCTION

Heart Failure (HF) has a prevalence of approximately 10% in the elderly, and is a common cause of hospitalization and death in older adults.[1] Patients diagnosed with HF have a 30% risk of mortality at 3 years, and those hospitalized for HF face a substantially higher risk.[1] Patients with HF are classified as having reduced ejection fraction (i.e. ≤40%) or preserved ejection fraction (i.e. >50%).[2] Evidence-informed treatments can improve clinical outcomes in HF, and recommendations surrounding their use are published in clinical practice guidelines.[2,3,4,5] Class I/Level A recommendations are supported by strong evidence, and are associated with reduced hospitalization and mortality. Class I recommendations include the assessment of heart function and provision of self-care education for all patients with HF; for patients with reduced ejection fraction, Class I recommendations also include specific pharmacological and device

therapies.[2] However, studies show that the uptake of these guidelines by physicians into routine clinical practice remains slow and inconsistent.[6,7,8]

Implementation interventions are designed to bridge the gap between evidence and practice, and are broadly classified at the provider, organizational, or health systems levels. Interventions may be single or multifaceted.[9] Implementation success also depends on the intervention-development process and organizational context. While previous reviews have evaluated implementation interventions,[10,11,12] none, to our knowledge, have evaluated interventions within HF care or identified contextual factors associated with implementation success.

Accordingly, the primary objective of our review was to examine the effectiveness of implementation interventions in increasing physician adherence to the specified HF guideline recommendations. Our secondary objectives were to assess the effect of implementation interventions on clinical outcomes, and to identify process and contextual factors that influence implementation success.

METHODS AND ANALYSIS

The systematic review protocol is registered in the International Prospective Register of Systematic Reviews (PROSPERO: CRD42015017155), and published in a peer-reviewed journal.[13] The only deviation from the protocol was the inclusion of uncontrolled before-after studies.

Eligibility criteria

We included trials evaluating 1 or more interventions aimed at improving physician adherence to Class I HF guidelines, relative to usual care. Interventions were categorized by level (i.e. provider-, organization-, systems- level) and type (i.e. education, decision-support, financial

incentives) according to the Cochrane Effective Practice and Organization of Care (EPOC) taxonomy.[9]

Outcomes

While implementation interventions were targeted towards healthcare providers, outcomes were measured at the level of the patient (e.g. number of patients receiving guideline-appropriate care). Primary outcomes were process indicators, defined as measures that assess guideline-consistent activities undertaken by a provider.[14] The primary outcomes included the proportion of eligible HF patients who: were prescribed a guideline-recommended pharmacological treatment such as β-blockers, angiotensin-converting-enzyme inhibitors (ACEIs), angiotensin II receptor blockers (ARBs), or mineralocorticoid receptor antagonists (MRAs); were referred for implantable cardioverter defibrillator (ICD) and/or cardiac resynchronization therapy (CRT) consideration; were provided self-care education at discharge; and/or had their left ventricular ejection fraction (LVEF) quantified. Secondary outcomes were clinical outcomes such as HF-related hospitalizations, readmissions and mortality. In the absence of HF-specific clinical outcomes, we extracted and reported all-cause clinical outcomes.

Study design

We included randomized controlled trials (RCTs), cohort studies (with comparisons), controlled and uncontrolled before and after studies, and interrupted time series studies.

Study selection

We searched for all English language articles published since 1990 in MEDLINE, EMBASE, HEALTHSTAR, CINAHL, The Cochrane Library, The Campbell Collaboration, The Joanna Briggs Institute Evidence Based Practice Database, The Agency for Healthcare Research and

Quality (AHRQ) Evidence-based Practice Centers' Research Reports, and the University of York Centre for Reviews and Dissemination Database. Our primary search strategy used the terms: heart failure, guideline adherence, practice guideline, evidence-based medicine, implement (Appendix 1). Our secondary search included terms for each of the different EPOC intervention types and heart failure (Appendix 2). Two authors independently screened titles and abstracts, and then assessed select full-text articles according to the eligibility criteria.

Data extraction and management

Two authors independently extracted details about study design, statistical analysis, intervention, patient and provider characteristics, follow-up, and outcomes using the EPOC Data Collection Checklist.[9] In addition, the Process Redesign framework was used to extract and synthesize details on the intervention-development process, and relevant contextual factors.[15]

Assessment of risk of bias

In addition to identifying the limitations inherent within specific study designs, two authors independently applied design-specific criteria to assess the internal validity of studies retained for analysis. We used the criteria outlined in the EPOC Data Collection Checklist to evaluate RCTs, cluster RCTs, controlled before-after studies, and interrupted time series studies.[9] For cluster RCTs, we used the additional criteria of recruitment bias, loss of cluster, and incorrect analysis according to the Cochrane Handbook of Systematic Reviews of Interventions.[16] For cohort studies, we utilized the Cochrane Collaboration's Tool to Assess Risk of Bias in Cohort Studies.[17] For uncontrolled before-after studies, we used the National Institute of Health's Quality Assessment Tool for Before-After Studies With No Control Group.[18] Because our goal was to assess internal validity, we did not use tool criteria pertaining to applicability or external validity, precision, and quality of reporting. We categorized studies as low risk of bias if

1 criterion was not satisfied, medium risk if 2 to 3 criteria were not satisfied, and high risk if more than 3 criteria were not satisfied.

Data synthesis

We classified the implementation interventions according to the level targeted (provider, organization, and system) and the type of intervention (e.g. education, decision-support, audit-and-feedback, financial) using the EPOC Taxonomy.[9] An abbreviated version of the EPOC Taxonomy is presented in Table 1. We explored the suitability of a meta-analysis of the results within

each intervention category by first assessing clinical heterogeneity at face value on the basis of included patient populations, settings (inpatient/outpatient), intervention types, and outcome measures. We then assessed statistical heterogeneity using the I^2 statistic, defining substantial heterogeneity as I^2>75%. For studies not suitable for meta-analysis, we narratively synthesized results.[19,20] We performed vote counting for each outcome measure in each EPOC intervention category, by noting the number of studies reporting significant improvements compared to those with no significant improvements.

Table 1. Effective Practice and Organization of Care Taxonomy

Intervention	Description
Provider Level	
Education	Distribution of educational materials; education sessions; or education outreach visits to providers
Audit and Feedback	Summary of clinical performance over a specified period with or without recommendations for clinical action. Information was obtained from medical records, computerized databases, or patients' observations
Reminders	Patient- or encounter- specific information provided verbally, on paper, or on a computer screen to prompt health professionals perform or avoid certain action
Organization Level	
Changes in medical	Modification of existing medical records systems (e.g. changing from

records systems	paper to computerized records)
Clinical multidisciplinary teams	A team of health professionals of different disciplines who work collaboratively to care for patients
Clinical pathways	Evidence-based care management tool for a specific group of patients with a predictable clinical course
Continuity of care	Formal arrangements for community-based assessment and treatment after hospital discharge
Systems Level	
Provider financial incentives/penalties	Financial reward or penalty for specific action by an individual provider
Institutional financial incentives/penalties	Financial reward or penalty for specific action by an institution or group of providers

Contextual factors

Context generally refers to the physical, social, political, and economic influences on healthcare practices.[21] We used the Process Redesign framework to systematically evaluate contextual factors that may influence the effectiveness of implementation interventions.[15] The Process Redesign framework classifies context into categories: outer setting, inner setting, and characteristics of individuals and teams. The inner context refers to the structural characteristics of the clinical setting (e.g. inpatient, outpatient, community-based care, academic status), networks and communications, culture, and climate. The characteristics of individuals and teams more specifically refer to professional roles, responsibilities, and authority within the organization. The outer context refers to factors related to the broader social, political, and economic environment in which the intervention is applied. We considered processes that introduced and adapted the intervention to the organization as part of the intervention, rather than the context. An abbreviated and modified version of the framework is presented in Table 2.

Table 2. Adapted Process Redesign Framework

Construct	Description
Process of Implementation (applied here as an intervention factor)	
Planning	Degree to which intervention steps are developed in advance of implementation and with consideration of various possible scenarios
Assessing	Formal assessment of the problem or condition to be changed, including needs of users, and barriers and facilitators of change
Staging and iteration	Whether the implementation is carried out in incremental steps, refined iteratively, or implemented in its entirety within a specified period
Access to information, training, and education	Staff access to information or education about the intervention
Inner Setting (contextual factor)	
Team and network characteristics	Influence, breadth, depth, and role diversity of teams and networks engaged in the Process Redesign
Teams, networks, and communications	Quality of teams and social networks; formal/informal communication and information exchange within an organization or between organizations
Culture	Norms, values, and beliefs within a team, unit, or practice that affect views of process redesign and its implementation
Mandate	Whether adherence to the intervention is expected or mandated
Leadership commitment	Degree of commitment, involvement, and accountability of leaders and managers to quality improvement and to the specific intervention
Human factors	Whether features of the physical and technical environment of the practice are designed to optimize human use, accessibility, and uptake in patient care
Outer Setting (contextual factor)	
External networks	Degree to which an organization is networked with other organizations engaged in similar types of process redesign activities
External pressure	Pressure emanating from outside the organization to introduce an intervention
External policy and incentives/disincentives	Laws, regulations, governmental recommendations, and/or payment schemes that affect the decision to adopt or abandon the process redesign efforts
Characteristics of Individuals and Teams (contextual factor)	
Role	Individual's or team's role and responsibilities, and the extent of multiple or shared roles
Authority	Perceived and actual degree of authority to make decisions and act autonomously

RESULTS

Identification, screening, and selection of studies

Our systematic search produced 3742 unique articles, of which 3590 were excluded on the basis of title and/or abstract review. We assessed 152 full-text articles, of which 38 studies met eligibility criteria. We excluded articles that: were abstracts, protocols, or letters (N=17); did not test implementation interventions (N=26); did not focus on HF patients (N=4); had no comparator group (N=6); or had no outcomes of interest (N=61) (see Figure 1).

Fig 1. PRISMA flow diagram of study selection

Characteristics of included studies

Setting. A majority of the studies were conducted in the USA (N=26), and the remainder in Europe (N=10) and Australia (N=2). Sixteen studies were conducted in inpatient settings, 21 in outpatient settings, and 1 involved care in both settings (Table 3).

Table 3. Summary of studies evaluating strategies for the implementation of Heart Failure (HF) clinical guidelines

Author (year) Country	Setting	Study design	Unit of recruitment / analysis (N)	Intervention and Process of Implementation (when described)	Process outcomes *	Clinical outcomes *
Professional Interventions						
Education						
Thilly et al. (2003) France	Tertiary care; inpatient	Cluster RCT	Hospitals (20)/Patients (370)	**Intervention:** Cardiologists presented guidelines and discussed cases with colleagues. Educational aids and guideline booklets were supplied to physicians. **Control:** Usual care; no implementation intervention. **Process:** *Planning/Assessment* – Prior to developing the educational intervention, a preliminary survey was conducted to identify specific guideline deviations in practice. Guidelines determined to be of particular concern were made the focus of the intervention.	**Target ACEI +27%[a], p=0.003**	
Asch et al. (2005) USA	Tertiary care; inpatient	Controlled Before-after	Patients (489)	**Intervention:** Provider teams attended 3 training sessions where national Quality Improvement and HF experts guided them in studying, testing, and implementing systematic improvements in HF care processes. **Control:** Usual care; no implementation intervention.	**ACEI +18%[b], p<0.0001**; β-blockers - 2%[b], P=0.49; LVEF +3%[b], p=0.49	
Audit and Feedback						
Kasje et al. (2006) Netherlands	Primary care	Cluster RCT	Providers (57)/Patients (508)	**Intervention:** Providers received patient-specific feedback on a sample of patients, and attended structured meetings to discuss guidelines and current management, identify problems, and propose	ACEI +5%[a], p>0.05	

				solutions for improving HF patient care. **Control:** Providers received education on management of type II diabetes. **Process:** *Planning/Assessment* – Optimal intervention design was determined through literature review. Specific barriers to guideline adherence were identified by physicians during peer-review meetings as part of the intervention.		
Frijling et al. (2003) Netherlands	Primary care	Cluster RCT	Practices (124)/Patients (236)	**Intervention:** Physician assistants provided physicians with a practice-specific feedback report, identified areas needing improvement, and provided guidance and resources for improvement. **Control:** Usual care; no implementation intervention.	Education odds ratio 0.85, p=0.636	
Cancian et al. (2013) Italy	Primary care	Before-after	Patients (1905)	**Intervention:** Performance data was aggregated across 21 health units. Project leaders reviewed data and identified barriers to unit leaders, who conveyed the data to all physicians involved. **Control:** Usual care; no implementation intervention. **Process:** *Access to information, training, education* – Intervention explained to participating physicians through two health unit training meetings.	**ACEI +3.6%[a], p=0.008; β-blockers +10.8%[a], p<0.0001**	
Matthews et al. (2007) USA	Tertiary care; outpatient	Before-after	Patients (265)	**Intervention:** Following discharge of patients from the hospital, outpatient physicians were provided quality-of-care reports outlining services received in hospital and areas for HF care improvement. This included instructions for medication titration and detailed HF education.	**ACEI +6.4%, p=0.042[a]**; β-blockers -1.1%[a], p=0.73; MRA	

				Control: Usual discharge information.	+11.1%[a], p=0.26	
Reminders						
Ansari et al. (2003) USA	Primary care	RCT	Patients (115)	**Intervention:** In addition to education on β-blocker use, physicians received a list of their HF patients eligible for β-blockers as well as electronic alerts when accessing patients' EMRs for first 2 visits after randomization. **Control:** Education on the use of β-blockers via Grand Rounds presentations and guideline dissemination. **Process:** *Planning/Assessment* – The intervention was designed to address a barrier identified at baseline.	β-blockers - 17%[a], p>0.05; Target β-blockers - 8%[a], p>0.05	HF-related hospitalizations +4%[a], p>0.05; 1-year all-cause mortality - 12%[a], p=0.05
Braun et al. (2011) Germany	Primary care	Before-after	Patients (190)	**Intervention:** Computer-based system displayed a pop-up window of a condensed version of the HF guidelines during clinical consultations. **Control:** Usual care; no implementation intervention.	ACEI - 4.4%[a], p=0.3; **β-blockers +12.3%[a], p=0.03**; **MRA +9.2%[a], p=0.04**	
Butler et al. (2006) USA	Tertiary care university hospital; inpatient	Before-After	Patients (1275)	**Intervention:** Computerized physician order entry system provided point-of-care reminders for select quality measures and included a prescription writer function. **Control:** Usual order entry form without disease-specific prompts.	ACEI +13%[a], p=0.10; **Education +53%[a], p<0.001**; LVEF	

				Process: *Planning/Assessment* – The intervention was developed iteratively prior to the intervention phase of the study. The program was modified based on institutional requirements, developer-initiated improvements, and user feedback.	+5%[a], p=0.86	
Qian et al. (2011) USA	Tertiary care university hospital; inpatient	Before-after	Patients (5000)	**Intervention:** Computer program flagged eligible patients not receiving ACEI/ARB. Pharmacists verified the flags and notified the medical team via EMR. Patients were re-flagged if no action was taken within 24 hours. **Control:** Usual care; no implementation intervention. **Process:** *Planning* – Comprehensive Plan-Do-Study-Act cycle occurred over a period of 1 year prior to the intervention phase. Problems were identified in the system's operating process and adjusted to increase work-flow efficiency.	**ACEI +9.2%[a], p<0.002**	
Gravelin et al. (2011) USA	Cardiology clinics; outpatient	Before-after	Patients (6632)	**Intervention:** EMR screening tool identified patients with left ventricular ejection fraction <35% and prompted cardiologists to refer to electrophysiologist for consideration of Internal Cardioverter Defibrillator (ICD) and/or Cardiac Resynchronization Therapy (CRT). **Control:** Usual care; no implementation intervention.	**ICD/CRT referral: site 1 +47%[a], p<0.02**; **site 2 +40%[a], p<0.001**	
Organizational Interventions						
Changes in medical records systems						
Reingold et al. (2007) USA	Tertiary care university	Before-after	Patients (171)	**Intervention:** Existing HF order sets were modified to be more succinct and visually organized, with the addition of narrative information to encourage utilization.	**ACEI +58%[a], p=0.008**	

	hospital; inpatient			**Control:** Routine order sets. **Process:** *Planning/Assessment* – The improvement process was initiated 5 years in advance of intervention phase, and the intervention was developed based on staff feedback.		
Oujiri et al. (2011) USA	Tertiary care university hospital	Before-after	Patients (153)	**Intervention:** A discharge face sheet embedded into the EMR reminded physicians of evidence-based measures and required physicians to indicate reasons for unmet measures. **Control:** Computerized order-entry form included reminders to address each diagnosis, but no prompts to follow treatment guidelines. Discharge orders were not easily accessible within the EMR, making it difficult to assess adherence to HF quality measures. **Process:** *Planning/Assessment* – The institution's admission and discharge processes were reviewed extensively to identify barriers to guideline-adherence at baseline, and these were addressed in the intervention design.	**ACEI +18%[a], p<0.01**; Education +5%[a], p>0.05; LVEF +12%[a], p>0.05	
Baker et al. (2011) USA	Primary care	ITS	Patients (276)	**Intervention:** Pre-visit paper reminders of outstanding quality deficits were printed and placed outside the patient's examination room to supplement existing electronic reminders within the EMR. **Control:** Electronic system offered point-of-care reminders, captured contraindications and patient refusals, and generated lists of patients not receiving essential medications.	ACEI +0% per year[c], p=0.95; **β-blockers +2.9% per year[c], p=0.004**	

				Process: *Planning/Assessment* – Following earlier introduction of an electronic reminder system, physician adherence to guideline recommendations was evaluated. Reasons for gaps were identified among a subset of physicians and addressed in the design of the paper intervention.		
Persell et al. (2011) USA	Primary care	ITS	Patients (not clear)	**Intervention:** An existing reminder system was updated to be minimally intrusive and include standardized means to capture contraindications. **Control:** EMR generated interruptive "pop-up" reminders at point of care, and did not possess a mechanism to record contraindications. **Process:** *Planning/Assessment* – Limitations in the EMR system were identified at baseline and addressed in the system re-design.	**ACEI +5.3% per year[c], p<0.001**; **β-blockers +5.7% per year[c], p<0.001**	
Clinical multidisciplinary team						
McCarren et al. (2013) USA	Tertiary care; outpatient	Cluster RCT	Hospitals (12)/Patients (220)	**Intervention:** Pharmacists were asked to invent methods to improve prescribing practices. Pharmacists received data on facility guideline adherence, along with a list of patients with suboptimal HF therapy. **Control:** Pharmacists were asked to invent methods to improve prescribing practices. Pharmacists received data on facility guideline adherence. **Process:** *Planning* – Intervention methods were designed to be pragmatic (i.e. data collection and presentation required by each pharmacist was minimal to promote participation)	Target β-blockers +1%[a], p>0.05	
Mejhert et al.	Tertiary	RCT	Patients (208)	**Intervention:** A nurse monitored patients after	**Target**	4-year all-

(2004) Sweden	university hospital; outpatient			discharge and adjusted their medications under the supervision of a senior cardiologist. **Control:** Conventional follow-up in primary care.	**ACEI +14%[a], p<0.05**; ACEI -5%[a], p>0.05; β-blockers -6%, p>0.05	cause mortality +7%[a], p>0.05 4-year all-cause readmissions +0%[a], p>0.05
Kasper et al. (2002) USA	Tertiary university hospital; outpatient	RCT	Patients (200)	**Intervention:** In the intervention group, HF nurses closely followed up with patients post-discharge and implemented the cardiologist-developed treatment algorithm. The control group received care from the primary physician alone. **Control:** Conventional follow-up in primary care.	ACEI +12.3%[a], p=0.07; β-blockers +8.1%[a], p=0.27;	
Ansari et al. (2003) USA	Primary care at a university hospital; outpatient	RCT	Patients (105)	**Intervention:** In addition to receiving education on β-blocker use, NPs, under physician supervision, were responsible for initiating, titrating, and maintaining eligible HF patient on β-blockers. **Control:** All providers received education on the use of β-blockers via Grand Rounds presentations and guideline dissemination. **Process:** *Planning/Assessment* – The intervention was designed to address a barrier identified at baseline.	**β-blockers +32%[a], p<0.001; Target β-blockers +33%[a], p<0.001**	HF-related hospitalizations -1%[a], p=0.66 1-year all-cause mortality -5%[a], p=0.05
Güder et al (2015) Germany	Tertiary university hospital; outpatien	RCT	Patients (390)	**Intervention:** HF-specialist nurses closely followed up with patients post-discharge and uptitrated medications under cardiologist supervision. **Control:** Conventional follow-up in primary care.	**ACEI +4.9%[a], p<0.05; Target ACEI**	

	t				**+25.1%[a], p<0.001; β-blockers +7.4%[a], p<0.05; Target β-blockers +23.9%[a], p<0.001;** MRA +5.7%[a], p>0.05; Target MRA +0.3%, p>0.05	
Warden et al. (2014) USA	Tertiary care; inpatient	Before-after	Patients (150)	**Intervention:** Pharmacists reviewed patients' records, addressed prescription concerns to the primary care team, and made suggestions for medication treatment and monitoring. **Control:** Usual care; medication reconciliation and patient management by physicians and nurses.	**ACEI +13%[a], p=0.02; Education +17%[a], p=0.007**	30-day HF-related readmissions -12%[a], p=0.11 **30-day all-cause readmissions -21%[a], p=0.02**
Martinez et al. (2013) USA	HF clinic; outpatient	Before-after	Patients (144)	**Intervention:** Pharmacists managed a clinic in which they initiated and adjusted medication dosages based on clinical characteristics. **Control:** Usual care; medication titration conducted by cardiologists.	**Target ACEI +21.9%[a], p=0.007; Target β-blockers +24.3%[a],**	

				Process: *Planning/Assessment* – The intervention was introduced to address previously identified gaps in HF care	**p=0.012**	
Crissinger et al (2015) USA	HF clinic; outpatient	Cohort	Patients (899)	**Intervention:** Nurse-practitioners and pharmacists adjusted medication dosages based on clinical characteristics, under HF physician supervision. **Control:** Patients were managed by general cardiologists.	ACEI +6%[a], p>0.05; **>50% Target ACEI +10%[a], p<0.0167; β-blockers +44%[a], p<0.0167; >50% Target β-blockers +43%[a], p<0.0167**	
Clinical pathways						
Panella et al. (2005) Italy	Tertiary care; inpatient	RCT	Patients (68)	**Intervention:** An integrated care pathway displayed patient care goals and provided the sequence and timing of actions necessary to achieve goals. **Control:** Usual care; no implementation intervention. **Process:** *Information, training, and education* – The intervention group received training to use the pathway *Planning/Assessment*: There was a 6-month planning period prior to the intervention phase to build work teams, review practices, develop the pathway, and perform ongoing evaluation and improvement.	ACEI +8.28%[a], p>0.05; **Education +27.7%[a], p<0.01**; **LVEF +35.4%[a], p<0.01**	30-day all-cause readmissions -4.36%[a], p>0.05 **30-day all-cause mortality -7.33%[a], p<0.05**

Garin et al. (2012) Switzerland	Tertiary care; inpatient	Before-after	Patients (363)	**Intervention:** A computerized clinical pathway included order sets for each stage of the hospital stay and required specific evaluation, treatment, and education criteria to be met prior to the next stage. **Control:** Usual care; no implementation intervention.	Target ACEI +0.2%[a], p=0.97; **β-blockers +14.3%[a], p=0.006**; **LVEF +16%[a], p=0.002**	30-day all-cause mortality -0.4%[a], p=0.8; 90-day all-cause mortality -0.8%[a], p=0.11 30-day all-cause readmissions -6.6%[a], p=0.11; 90-day all-cause readmissions -8.2%[a], p=0.11
Whellan et al. (2001) USA	HF clinic; outpatient	Before-after	Patients (117)	**Intervention:** Based on predefined protocols and severity of the patient's illness, a follow-up schedule for clinic visits and telephone calls was initiated at the time of enrolment. **Control:** Usual care; no implementation intervention. **Process:** *Access to information, training, and education* – Pre-enrollment, internal medicine house-staff and primary care physicians in the network were presented an outline of the program; pocket cards with inclusion criteria and referral phone numbers were also provided for all nursing stations at the	**β-blockers +24%[a], p<0.01**; **Target β-blockers +7%[a], p<0.01**; ACEI +1%[a], p=0.75	**1.5 (control) vs. 0 (intervention) all cause hospitalizations per patient-year, p<0.01**

				hospital. *Planning/Assessment* – The program was designed by adapting practices from other disease management programs to the needs of the local health system.		
McCue et al. (2009) USA	Tertiary care; inpatient	Cohort	Patients (6013)	**Intervention:** A clinical pathway comprised an order sheet, clinical outcomes monitoring checklist, explanations for nursing, and disease-specific patient education forms. **Control:** Usual care; no implementation intervention. **Process of implementation:** *Planning/Assessment* – Design of the clinical pathway was dynamic; practitioner feedback was continuously sought and incorporated into pathway design throughout the intervention period.	**ACEI +17.2%[a], p<0.001**; **LVEF +10.6%[a], p<0.001**	
Ranjan et al. (2003) USA	Tertiary care; inpatient	Cohort	Patients (371)	**Intervention:** A clinical pathway for HF care was implemented. **Control:** Usual care; no implementation intervention.	**ACEI +33%[a], p<0.001**	
Continuity of Care						
Hickey et al. (2016) Australia	HF Clinic; outpatient	Cohort	Patients (335)	**Intervention:** HF disease management clinic facilitates communication between hospital and primary care by means of a comprehensive medication titration form outlining recommended target dose of medications, the order of titration, and primary clinician responsible for managing titration. **Control:** Discharge titration form was available, but rarely used to facilitate patient transition from hospital to community.	Target ACEI +11%[a](2010), +18%[a](2011), p=0.051**; Target β-blockers -5%[a](2010), +13%[a](2011), p=0.045**	

				Process: *Planning/Assessment* – A steering committee comprised of cardiologists, general practitioners, pharmacists, and nurses met quarterly to refine the implement the intervention in an iterative Plan, Do, Study, Act (PDSA) cycle. Barriers and solutions were developed by interviewing physicians and practice managers.		
Financial Interventions						
Provider incentives						
Esse et al. (2013) USA	Tertiary care; inpatient	Cohort	Patients (4304)	**Intervention:** Primary physicians responsible for patients in the Medicare Advantage Prescription Drug Plan were financially compensated for utilization of evidence-based HF therapy. **Control:** Usual care; no implementation intervention.	ACEI – 1.85%[a], p=0.244; β-blockers - 0.06%[a], p=0.972	All-cause hospitalizations: acute visits +2.58%[a], p=0.100; ER visits +0.62%[a], p=0.675
Institutional incentives						
Lindenauer et al. (2007) USA	Tertiary care; inpatient	Controlled Before-after	Patients (50678)	**Intervention:** Hospitals submitted data on 33 HF quality measures. Those performing in the top decile for a given year received a 2% bonus payment in addition to usual Medicare reimbursement. **Control:** Usual care; no implementation intervention.	ACEI +2%[b], p=0.34; **LVEF +5.1%[b], p<0.001**	
Sutton et al. (2012) England	Tertiary care; inpatient	Controlled Before-after	Patients (not clear)	**Intervention:** Hospitals submitted data on 28 HF quality measures. At the end of the first year, hospitals that reported quality scores in the top quartile received a 4% bonus. **Control:** Usual care; no implementation intervention.	ACEI +1.4%[b]; LVEF +8.1%[b]; no p-values reported Education +15.2%[b]	30-day all-cause mortality - 0.6%[a], p=0.3

Combined Interventions						
Peters-Klimm et al. (2008) Germany	Primary care	Cluster RCT	Providers (37)/Patients (168)	**Intervention:** Physicians engaged in 4 didactic, interdisciplinary educational meetings with primary care physicians, cardiologists, and psychosomatic specialists; and received pharmacotherapy feedback (% target dose) on individual patients. **Control:** Physicians received a standard lecture on guideline-recommended treatment of HF. **Process:** *Information, training, and education* – Physicians received initiation visit, which included an introduction to the intervention and a handout of the trial investigator file. *Opinion leaders* – Education component of the intervention was provided by a senior cardiologist with didactic expertise.	ACEI +8.7%[a], p=0.15; **Target ACEI +12.3%[a], p=0.04**; β-blockers -4.8%[a], p=0.67; Target β-blockers +1.7%[a], p=0.26	
Fonarow/Gheorghiade et al. (2010/2012) USA	Cardiology clinic; outpatient	Before-after	Patients (15 177)	**Intervention:** The intervention consisted of a guideline-based clinical decision support tool kit, educational materials, practice-specific data reports, benchmarked quality-of-care reports, and structured educational opportunities. **Control:** Usual care; no implementation intervention. **Process:** *Information, training, and education* – A 1-day workshop for practice personnel provided overview of study goals and tool kit. *Planning/Assessment* – A steering committee was appointed to follow a structured, rigorous, guideline-driven process to develop the pathways and tools prior to the intervention phase. *Opinion leaders* – The educational component of the	**ACEI +6.7%[a], p<0.001**; Target ACEI +1.8%, p=0.053[a]; **β-blockers +7.4%[a], p<0.001**; Target β-blockers +9.8%, p=<0.001; **MRA +27.4%[a],**	

				intervention included expert opinions regarding best practices in HF care.	**p<0.001**; Target MRA +4.1%, p=0.107; **Education +9.1%[a], p<0.001**; **ICD referral +30.3%[a], p<0.001**	
Goff et al. (2005) USA	Primary care	Before-after	Patients (3141)	**Intervention:** Physicians received performance audit and feedback, aggregated across a multicounty health service area; and patient-specific chart reminders regarding medications and education. **Control:** Usual care; no implementation intervention. **Process:** *Planning* – The intervention planning team identified and addressed barriers at provider and patient levels. *Patients* – The intervention planning team developed an educational brochure based on results of focus groups with HF patients.	ACEI -2.7%[a], p=0.26; **β-blockers +15.2%[a], p<0.0001**; **LVEF +4.3%[a], p<0.0001**	

Riggio et al. (2009) USA	Tertiary care; inpatient	Before-after	Patients (4728)	**Intervention:** The intervention consisted of a computerized discharge checklist with electronic prompts on medication use, LVEF assessment, and discharge instructions; personalized resident performance reports; financial bonus for residents achieving a threshold of quality compliance; lectures on hospital/state/nation quality performance. **Control:** Usual care; no implementation intervention. **Process:** *Planning* – The intervention planning team received and incorporated ongoing feedback from residents and physicians in developing the reminder system prior to the intervention phase.	**ACEI +15.7%[a], p<0.001**; **Education +55.8%[a], p<0.001** LVEF -0.2%[a], P=0.78	
Scott et al. (2004) Australia	Mixed; Tertiary and primary care practices	Before-after	Patients (904)	**Intervention:** The in-hospital component consisted of: reminders on patient charts; clinical pathways for emergency chest pain assessment and management; educational presentations as grand rounds, seminars, workshops, and case-based meetings; briefing of hospital and primary care physicians by clinical pharmacists. The discharge-planning component consisted of standardized discharge referral summaries with personal treatment targets; medication lists forwarded to community pharmacists; pharmacist counselling of patients about lifestyle changes, drug therapy, and risk-factor modification; post-discharge telephone follow-up by clinical pharmacists of high-risk patients. **Control:** Usual care; no implementation intervention. **Process:** *Planning/Assessment* – Intervention was designed to address several implementation barriers	**ACEI +15%[a], p=0.04; β-blockers +21%[a], p=0.01**; LVEF +9%[a], p=0.06	30-day HF-related readmissions +0.8%[a], p>0.05 **All cause mortality: 30-day -2.9%[a]; p<0.04, 6-month -7.6%[a], p<0.001**; **and 1-year all-cause mortality +10.4%[a], p=0.005**

				that were identified through literature review.		
Dykes et al. (2005) USA	Tertiary care; inpatient	Before-after	Patients (314)	**Intervention:** This involved a clinical pathway in EMR; a HF self-management education tool; and ongoing performance feedback. **Control:** Usual care; no implementation intervention.	Medication prescription +6.4%[a], p=0.389; **Education +64.9%[a], p=0.000**	

*Statistically significant results are shown in bold letters. [a]Absolute risk difference reported as (intervention group – control group). [b]Difference in difference (controlled before/after studies) reported as [intervention group (Time 2 – Time 1) – control group (Time 2 – Time 1)]. [c]Difference in rate of change (ITS studies) reported as (intervention group rate of change – control group rate of change). EMR, electronic medical record; NP, nurse practitioner; ACEI, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; MRA, mineralocorticoid receptor antagonist; LVEF, left ventricular ejection fraction.

Types of implementation interventions. Thirteen studies offered interventions directed at the level of healthcare providers, 18 at the organization level, 3 at the health system level, and 4 across multiple levels. Provider-level interventions included: audit and feedback (N=4 studies),[22-25] reminders (N=5),[26-30] education (N=2),[31,32] and a combination of these (N=2).[33,34] Organization-level interventions included: changes in medical records systems (i.e. adaptations to existing systems on the basis of organizational need) (N=4),[35-38] clinical multidisciplinary teams (N=8),[26,39-45] clinical pathways (N=5),[46-50] and continuity of care (N=1).[51] System-level interventions included: financial incentives for providers (N=1) [52] and financial incentives for institutions (N=2).[53,54] Four studies offered interventions across multiple levels. A common feature across all 6 multifaceted interventions was the use of audit and feedback (Table 3).

Study design. Among the 38 studies included, 10 were RCTs. Five were randomized at the level of patients,[26,39,40,44,46] and 5 were cluster randomized by practice or hospital.[22,23,31,33,41] Twenty-three studies used quasi-experimental designs: 3 were controlled before-after studies,[32,41,53] 2 were interrupted time series studies,[34,35] and 18 were uncontrolled before-after studies.[24,25,27-30,34-38,42,43,47,48,55,56] Four studies used a retrospective cohort design,[45,49,50,52] while 1 used a combination of retrospective and prospective cohort designs[51] (see Table 3).

Risk of bias. Most studies were deemed to have medium risk of bias when assessed using design-specific criteria (Appendix 3). Five patient-level RCTs,[26,39,40,44,46] and 4 of the 5 cluster RCTs had low risk of bias.[23,31,33,46]

Quality of reporting. We evaluated the quality of reporting in RCTs using the CONSORT statement, including the extension for cluster RCTs. Among the 5 RCTs, 4 did not provide

information on the methods of randomization or allocation concealment.[26,39,44,46] None of the 5 studies reported the precision of effect size estimates or provided relative effect sizes in addition to absolute risk differences.[26,39,40,44,46] Among the 5 cluster RCTs, 4 did not provide information on the methods of randomization or allocation concealment,[22,31,33,41] 3 did not describe eligibility criteria,[20,21,29] 3 did not provide sample size calculations,[22,33,41] and 4 did not provide intra-cluster correlation values.[22,23,31,41]

Outcomes reported. Thirty-seven studies reported the proportion of patients prescribed recommended medications (i.e. ACEI/ARBs, β-blockers, MRAs); 30 studies reported prescription of indicated medications at any dose,[22,24-26,28,29,33-40,42,44-50,52-54,57-59] and 12 reported prescriptions of medications at target doses.[26,31,33,39,41,43-45,47,48,51,56] Other studies reported: patient self-care education prior to discharge (N=9);[23,27,38,42,46,54,55,57,59] referrals for ICD/CRT (N=2),[30,55] and LVEF assessments (N=11).[27,33,34,38,46,47,49,53,54,57,58] In addition to these primary outcomes, 11 studies reported clinical outcomes such as mortality, hospitalization, and readmission rates.[26,32,39,40,42,44,45,46,49,51,55] I^2 calculations produced a value greater than 80% for most categories of interventions, precluding the possibility of a meta-analysis. Therefore, the studies were synthesized narratively.

Effectiveness of Implementation Interventions

A summary of study outcomes is presented in Table 3. A majority of studies (n=32, 84%) reported significant improvements in at least one primary outcome.

Prescription of indicated medications. Reminders, clinical pathways, changes in medical records systems, and multifaceted interventions were commonly associated with an increase in guideline-recommended prescriptions. In 4 studies that reported prescriptions of more than 1

indicated medication, significant improvements were observed in the prescription of β-blockers and MRAs, but not in the prescription of ACEIs. In these studies, the prescription rates at baseline for ACEIs were substantially higher than those of β-blockers or MRAs, ranging from 78.0% to 86.3%.[28,34,36,48]

Reminders. Two of 4 studies on reminders within electronic medical records (EMRs) reported a significant increase in the percent of patients prescribed an indicated medication.[28,29] One study in which reminders were unsuccessful had suboptimal intervention fidelity; stratification by actual use of the reminder system revealed a significant improvement in prescription rates.[27]

Clinical pathways. Four of 5 studies on clinical pathways reported a significant increase in the percent of patients prescribed an indicated medication.[47-50] The single study that reported no significant change was an RCT in a remote community hospital, in contrast with the urban and/or teaching hospital settings of other clinical pathway studies.

Medical records systems. All four studies evaluating changes to EMRs reported significant increases in the percent of patients prescribed an indicated medication.[35-38] In each of these interventions, existing EMRs were enhanced by addressing identified limitations (Table 3).

Combination interventions. Two studies evaluated combinations of provider-level interventions. A combination of education with audit and feedback did not significantly increase the percent of patients prescribed an indicated medication,[33] while a combination of education, reminders, and audit and feedback did.[34]

Four studies combined implementation interventions across different levels of the EPOC taxonomy.[55-59] Two studies combined clinical pathways with audit and feedback; 1 reported a

significant increase in the percent of patients prescribed an indicated medication.[55] Another study that combined a computerized order set, reminders, audit and feedback, financial incentives, and provider educational meetings, also reported a significant increase in the percent prescribed an indicated medication. [57] Finally, an intervention that fostered hospital-community integration using a combination of reminders, education for providers, audit and feedback, discharge summaries, and patient follow-up by pharmacists [58] reported a significant increase in β-blocker prescriptions in-hospital, and in all medications 6-months post-discharge.

Prescription of target-dose medications. Clinical multidisciplinary team interventions were consistently successful in increasing prescription of target-dose medications, with 5 of 6 studies reporting significant improvements for this outcome.[26,39,43-45] The 5 successful clinical multidisciplinary team interventions - including 3 RCTs [26,39,44] - involved nurses or pharmacists initiating or titrating medications according to a protocol. Among these studies, the absolute increase in proportion of patients prescribed target-dose ACEIs ranged from 10% to 25.1%.[39,43-45] The absolute increase in proportion of patients prescribed target-dose β-blockers ranged from 23.9% to 43%.[26,44,45] In contrast, an unsuccessful intervention tasked pharmacists with improving prescribing practices, without clearly defining the mechanism to do so.[41]

One of 2 studies [47,48] evaluating clinical pathways reported a significant increase (from 6% to 13%) in prescription of target-dose β-blockers.[48] Of the two studies evaluating multifaceted interventions, an intervention combining education with audit and feedback reported a significant improvement (from 44% to 72%) in the prescription of target-dose ACEIs, [33] while a comprehensive intervention combining education, reminders, audit and feedback, and clinical

pathways did not report significant improvements.[56] In the successful multifaceted intervention, feedback was focused strictly on medication dosing for individual patients.[33]

A study evaluating a continuity of care intervention, including the provision of instructions for medication titration to the outpatient general practitioner, reported a significant improvement (from 38% to 51%) in the prescription of target-dose β-blockers within 6 months of discharge, 51]

Provision of patient self-care education. Only 9 studies reported on the provision of self-care education to patients. Three multifaceted intervention studies reported this outcome measure, with a significant improvement in each case.[55,57,59] Provision of patient education also increased with a reminder system,[27] a clinical multidisciplinary team,[42] and a clinical pathway.[46] In contrast, interventions that did not produce significant improvements included: audit and feedback,[23] and changes to medical records systems.[38] One study, on financial incentives, did not report statistical significance.

LVEF assessment. Eleven studies reported the percent of patients who received an LVEF assessment. All three clinical pathway studies, including an RCT, reported significant improvements in this outcome.[46,47,49] Of the 2 studies evaluating institutional financial incentives [53,54], only 1 reported significant improvements.[53] Only 1 of 3 studies [34,57,58] evaluating multifaceted interventions that included audit and feedback as well as reminders reported significant increases in LVEF assessment.[34] Education,[32] reminders,[27] and changes in medical records systems,[38] did not significantly increase LVEF assessment

ICD/CRT referral. Only 2 studies measured the percent of indicated patients who received an ICD/CRT referral. These studies evaluated a reminder intervention,[30] and a multifaceted

intervention combining reminders, clinical pathways, education, and audit and feedback,[55] respectively, with significant improvements reported in each case.

Evidence from RCTs

Very few RCTs were available for most intervention types; none were available for medical records system changes or financial incentives. Five RCTs evaluated the effect of clinical multidisciplinary teams on overall prescription rates,[26,39,40,44] and target-dose prescriptions.[26,39,41,44] Among these, 2 of 4 reported significant improvement in overall prescription rates,[26,44] and 3 of 4 reported significant improvements in target-dose prescriptions.[26,39,44] Two RCTs evaluated audit and feedback interventions,[22,23] with no significant improvements in the reported outcomes. An RCT evaluating education [31] reported significant improvements for all outcomes measured, while an RCT assessing reminders [26] reported no significant improvements. The RCT evaluating a clinical pathway [46] significantly increased patient self-care education,[46] and the RCT assessing a multifaceted intervention significantly increased the prescription of some target-dose medications.[33]

Clinical outcomes

While 5 of the 6 studies reporting all-cause mortality successfully improved process outcomes, only 2 reported a significant decrease in mortality: an RCT evaluating a clinical pathway [46] and a before-after study assessing a multifaceted transitional care intervention.[58]

While all 6 studies reporting all-cause hospitalization or readmission rates improved process outcomes [32,39,42,46-48], significant improvements in the clinical outcomes were only reported in 2: a multidisciplinary team study [42] and a clinical pathway study.[48] Both studies used a before-after design with medium risk of bias. There was no improvement in 2 studies

assessing clinical pathways [46,47], 1 assessing multidisciplinary interventions [39], and 1 assessing an educational intervention.[32]

While 3 of 4 studies reporting HF-related hospitalizations or readmissions [14,34] improved process outcomes, none reported significant improvements in the HF-related clinical outcomes.

Process of implementation (Table 3)

Six studies reported provision of preliminary training, education, and resources to introduce clinicians to the implementation intervention and encourage utilization; in each case interventions were effective in improving at least 1 process outcome.[23,27,40,47,48] Nine studies assessed barriers to guideline implementation at baseline and adapted the interventions accordingly.[18,30,33,37,42,46,51,57] This was associated with implementation success for all interventions, with the exception of audit and feedback.[46] Seven studies used an iterative process, whereby the program was regularly updated on the basis of institutional requirements and user feedback.[28,34,36,40,51,56,59] An iterative intervention-development process was associated with implementation success across the range of interventions in which it was reported.

Contextual factors (Appendix 4)

Inner setting. Five interventions that improved at least 1 process outcome reported leadership support from either the department or hospital-level.[28,34,41,56,57]

Outer setting. In 9 US studies,[28-30,36-38,42,56,59] there were preexisting initiatives by the Centers for Medicare and Medicaid Services (CMS) or The Joint Commission (TJC), including financial reimbursements or accreditation on the basis of HF readmission rates, and public reporting of quality of care data. These contextual factors encouraged organizations to

implement interventions to improve guideline adherence. This is in contrast to the lack of success observed when financial interventions were used as the implementation intervention itself.

DISCUSSION

In this systematic review, we assessed the effectiveness of implementation interventions aimed at improving physician adherence to Class I HF guideline recommendations. We synthesized our findings narratively as the variation in study design, intervention, and outcomes across studies precluded meta-analysis.

We found that a majority (84%) of 38 studies reported significant improvements in at least 1 process outcome. A process outcome commonly reported across studies and interventions was the proportion of patients prescribed an indicated medication: 12 studies reported on the prescription of ACEIs,[22,27,29,37,38,42,46,49,50,53,54,57] 2 on the prescription of β-blockers,[26,47] 12 on the prescription of ACEIs and β-blockers,[24,32-35,39,40,45,48,52,58] and 4 on the prescription of ACEIs, β-blockers, and MRAs.[25,28,44,55] Electronic medical system interventions were associated with significant improvements in the prescription of at least 1 medication in 100% of studies (4/4 studies),[35,37,38,60] followed by clinical pathways (80%, 4 of 5 studies),[47-50] multifaceted interventions (66%, 4/6 studies),[34,55,57,58] and reminders (50%, 2/4 studies).[28,29] Very few studies on education or audit and feedback reported this outcome, making direct comparisons with other interventions challenging. However, on the whole, the results across a number of studies suggest that educational seminars,[30] and audit and feedback [20,21] are minimally effective in isolation. Audit and feedback appears to be an important component of multifaceted interventions, however,

[34,55,57,58] and it is possible that factors such as the type of feedback and co-interventions to address gaps in care can influence its effectiveness.[61]

Results from RCTs reinforced overall findings that clinical multidisciplinary teams, with clear pre-defined responsibilities, seem to be especially effective in titrating patients to their target dose.[26,39,40,41,44] These findings are important; despite evidence of dose-related improvements in hospitalization and mortality, only a small proportion of HF patients receive an appropriate dose of evidence-informed medications.[62,63,64] A study using registry data from 21 European and Mediterranean countries from 2011-2013 found that while ACEIs, β-blockers, and MRAs were used in 92.2, 92.7, and 67.0% of patients, respectively, only 30% of these patients received medications at the target dosage.[65]

In general, improvements in process outcomes as a result of implementation interventions, were rarely accompanied by improvements in clinical outcomes. In some studies, the gap between process and clinical outcomes may be attributed to insufficient statistical power to detect improvements in clinical outcomes.[13,25,33] The gap may also be explained by study designs that did not account for background trends or adjust for confounding variables. Finally, HF clinical outcomes are multifactorial and depend not only on the physician prescribing appropriate medications, but also on the patient's adherence to these medications, and follow-up care by other providers.[32] The studies that showed a trend toward reduction in HF-related readmissions, albeit not significant, are those that addressed more than 1 of these factors.[40,42]

The context in which an implementation intervention is applied can influence its success.[61,66] The limited contextual details available in the included studies made it difficult to identify facilitators of implementation efforts. In general, support of organization leaders, and external policies and incentives for guideline adherence seemed to be associated with guideline uptake.

These findings are consistent with results from a 2011 study that used iterative, formal discussions with leaders in patient safety and healthcare systems to identify leadership involvement and external factors (e.g. financial or performance incentives or patient safety regulations) as context domains important to quality improvement initiatives.[67]

Consistent with existing literature,[68,69] our results did not demonstrate a clear relationship between the number of intervention components and intervention success. An extensive review by Grimshaw et al. concluded that while multifaceted interventions are not inherently more effective than single interventions, they may be more effective when built upon a comprehensive assessment of barriers.[70-72] Among the studies on multifaceted interventions in our review, the 4 studies that reported significant improvements in medication prescription rates carefully considered barriers at baseline and sought user feedback throughout the intervention development process.[34,55-58]

Our results are concordant with recently published findings from the American Heart Association's comprehensive Get With The Guidelines (GWTG)-HF program, which used a combination of educational approaches, multidisciplinary teams, and public hospital performance reporting to improve care.[73] The intervention was carefully adapted and introduced at each hospital site through collaborative discussions of barriers and solutions, and iterative plan-do-study-act (PDSA) cycles prior to the intervention phase.[74]

There were a number of limitations to our review. First, the variation in interventions, settings, study designs, and outcome measures precluded meta-analyses, and in turn, our ability to draw substantive conclusions regarding specific implementation strategies and their comparative effectiveness. We chose to use a "vote counting" approach to synthesis. While this method is useful in presenting an initial description of the trends found across studies, it is limited by the

fact that it assigns equal weight to studies of varying sample sizes, effect sizes, and significance levels.[75]

Another limitation was the methodological quality of the primary studies. Most studies used observational and quasi-experimental study designs. Quasi-experimental and observational designs possess some inherent risks of bias. In uncontrolled before-after studies, which formed the majority of studies in this review, temporal trends or sudden changes make it difficult to attribute the observed effects to the intervention alone. A time-series design increases confidence with which the observed effect can be attributed to the intervention; however, it does not protect against simultaneous events that may influence the intervention effect. Controlled before-after studies can protect against these effects, but cannot match groups on the basis of unknown confounders. We found that most quasi-experimental and observational studies possessed at least a medium risk of bias. Though almost all included RCTs demonstrated low risk of bias, they were largely applied in the evaluation of multidisciplinary team interventions, and less so to the evaluation of other implementation interventions.

A minority of studies in this review (10 of 35 studies) were RCTs, considered the gold standard in establishing a causal link between an intervention and its outcome. Indeed, RCTs are an uncommonly used methodology in implementation studies. In a recent systematic review of implementation interventions for the management of ICU delirium, only 1 of the 21 studies was an RCT, 16 were before-after studies, and the remaining were cohort studies.[76] In another review on implementation interventions to improve the use of pain management assessments for hospitalized patients, only 3 of the 23 studies were controlled clinical trials, and the remaining 20 were uncontrolled before-after or time-series studies.[77] While randomized trials are robust in methodology, they pose a number of logistical challenges that may make them suboptimal for

implementation research; they are expensive and time consuming, often requiring years to complete.[78] Changes in health care delivery are often implemented under internal and external pressures that seek to resolve an institutional problem in the shortest time possible. Under such circumstances, quasi-experimental designs are often felt to be most feasible.[78,79] A solution may be found in pragmatic clinical trials – such as the stepped wedge cluster RCT - which can offer the methodological benefits of randomization while being sensitive to the challenges of implementation research.[80]

Another limitation was that many studies failed to provide adequate details on the intervention, context, barriers, facilitators, or fidelity to the intervention. A review by Proctor et al. explores the reporting challenges in implementation research in significant detail. It offers a theoretical discussion of principles for naming, defining, and specifying implementation interventions.[81]

Suggestions for future studies

We identify a number of ways in which future research on the effectiveness of implementation interventions may be strengthened. First, there is a need for implementation interventions to be evaluated using more robust study designs that also account for the pragmatic challenges of implementation research. Furthermore, reporting of studies should adhere to standardized guidelines in order to better facilitate comparison between interventions. An example of reporting guidelines is the Quality Improvement Minimum Quality Criteria Set (QI-MQCS), which spans the spectrum of intervention characteristics and contextual factors.[82]. Implementation research in HF may also benefit from more careful consideration of the contextual factors that influence implementation success. Finally, in addition to examining process outcomes, the direct impact of implementation interventions on clinical outcomes should be examined more consistently.

CONCLUSIONS

In this review, the heterogeneity of interventions, study designs, and outcomes limited our ability to draw substantive conclusions regarding the comparative effectiveness of implementation interventions. Trends observed across the included studies suggest that effective implementation interventions include electronic medical records systems, clinical multidisciplinary teams, clinical pathways, and multifaceted interventions that include audit-and-feedback. There is a need for higher quality research to assess the effectiveness of implementation interventions on HF care processes and on clinical outcomes, and for the use standardized reporting guidelines. Future work in the area should also include a closer examination of the organizational and external implementation context in order to better facilitate targeted application of implementation strategies.

Contributors: HGCV, IDG, and SJC conceived the study, and all authors contributed to the study design. DS contributed to the search strategy, extracted and synthesized study data, and drafted and edited the manuscript. IDG, KH, RBH, and SJC contributed intellectual input and edited the manuscript for critical content. IG contributed to the search strategy and extracted study data. HGCV informed the search strategy, synthesized study data, drafted and edited the manuscript, obtained research funding, and supervised the conduct of the study.

Acknowledgements: We thank Quazi Ibrahim for his help in assessing whether the study was amenable to meta-analysis.

Dedication: This work is dedicated to the memory of Aubrey Ignatius Van Spall, beloved father and friend.

Funding: This study was funded by Ontario's Ministry of Health and Long Term Care (MOHLTC) Health System Research Fund and Canadian Institutes of Health Research. IDG

receives support from a CIHR Foundation Grant. HGCV receives salary support from the MOHLTC and Hamilton Health Sciences Career Research Award.

Competing interests: We have read and understood BMJ policy on declaration of interests and declare that we have no competing interests.

Data Sharing Statement: All relevant study data can be found in the supplemental files.

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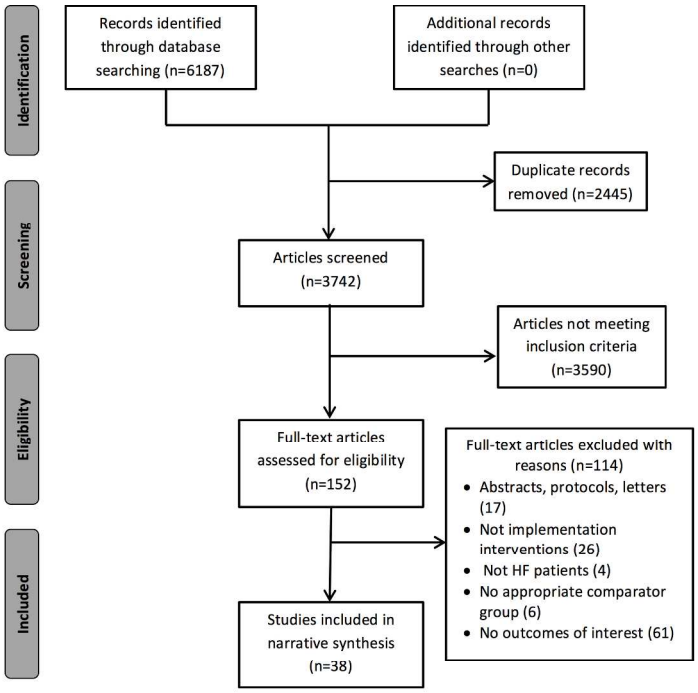

Fig 1. PRISMA flow diagram of study selection

215x279mm (300 x 300 DPI)

MEDLINE search strategy

1. exp Heart Failure/ or heart failure*.mp.
2. Guideline Adherence/ or guideline adherence*.mp.
3. practice guideline/ or practice guideline*.mp.
4. exp Evidence-Based Medicine/ or evidence based medicine*.mp. or evidence based practice*.mp.
5. implement*.mp. or standards.fs.
6. best practice*.mp
7. 1 and (2 or (5 and (3 or 4 or 6)))
8. limit 7 to (english language and yr="1990 -Current")

MEDLINE and EMBASE secondary search strategy

1. exp Heart Failure/
2. exp Cardiac Output, Low/
3. pay for performance.mp. or exp Reimbursement, Incentive/
4. clinical pathways.mp. or exp Critical Pathways/
5. clinical decision support system.mp. or exp Decision Support Systems, Clinical/
6. multidisciplinary team.mp.
7. Education, Medical, Continuing/ or educational interventions.mp.
8. (audit and feedback).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
9. Reminder Systems/ or reminders.mp.
10. 3 or 4 or 5 or 6 or 7 or 8 or 9
11. 1 or 2
12. 10 and 11
13. limit 12 to (english language and yr="1990 -Current")

Supplementary Table 1. Risk of bias among the RCTs and controlled before-after studies using the EPOC framework

Name, year	allocation concealment	Follow up of professionals	Follow up of patients	Blinded assessment of primary data	Base line measurement	Reliable primary outcome	Protection against contamination	Appropriate analysis	No Recruitment bias	No Loss of cluster	report of characteristics (2^{nd} control site)
Cluster RCT											
Frijling et al. (2003)	+	+	+	-	+	-	+	+	+	+	N/A
Kasje et al (2006)	+	+	+	+	+	+	+	+	+	+	N/A
Klimm et al.(2008)	+	+	+	+	+	+	+	+	+	+	N/A
McCarren et al.(2013)	+	+	+	+	+	+	+	+	+	+	N/A
Thilly et al.(2003)	+	+	+	+	+	+	+	+	+	+	N/A
RCT											
Ansari et al. (2003)	+	+	+	+	+	+	+	N/A	N/A	N/A	N/A
Kasper et al.(2002)	+	+	+	+	+	+	+	N/A	N/A	N/A	N/A
Mejhert et al. (2004)	+	?	+	+	+	+	+	N/A	N/A	N/A	N/A
Panella et al. (2005)	?	+	+	+	+	+	+	N/A	N/A	N/A	N/A
Güder et al. (2015)	+	+	-	+	+	+	+	N/A	N/A	N/A	N/A
Controlled Before-After											
Asch et al. (2005)	N/A	?	?	+	+	+	?	N/A	N/A	N/A	+
Lindenauer et al. (2007)	N/A	?	?	+	+	+	?	N/A	N/A	N/A	?
Sutton et al. (2012)	N/A	?	?	?	+	+	N/A	N/A	N/A	N/A	+

+, criteria met; -, criteria not met; ?, unclear; N/A, not applicable

Supplementary Table 2. Risk of bias among the interrupted time series using the EPOC framework

Name, year	protection against secular changes	Appropriate data analysis	Reason for the number of points pre and post	Shape of intervention effect specified	Protection against detection bias	Blinded assessment of primary outcome	Completeness of data set	Reliable primary outcome measure
Persell et al. (2011)	+	+	?	?	+	+	?	?
Baker et al. (2011)	+	+	?	?	+	+	+	+

+, criteria met; -, criteria not met; ?, unclear; N/A, not applicable

Supplementary Table 3. Risk of bias among the cohort studies using the Cochrane Collaboration framework

Name, year	Exposed/non-exposed from same group	Assessment exposure	Outcome of interest not present at study start	Matched for all prognostic variables or statistical adjustment	Assessment of presence/absence of prognostic factors	Assessment of outcome	Adequate follow up of cohorts	Similar co-interventions between groups
McCue et al. (2009)	+	+	+	?	?	+	+	?
Ranjan et al. (2003)	+	+	+	-	+	?	+	?
Esse et al. (2013)	+	+	+	+	+	+	+	?
Crissinger et al. (2015)	+	+	+	-	+	+	+	?
Hickey et al. (2016)	-	+	+	+	+	+	+	?

+, criteria met; -, criteria not met; ?, unclear; N/A, not applicable

Supplementary Table 4. Risk of bias among the uncontrolled before-after studies using the National Institute of Health framework

Name, year	Eligibility criteria prior to defined enrollment	Outcomes clear, valid, reliable	Blinding of outcome assessors	Follow up of providers (80%)	Follow up of patients (80%)	Statistical analysis	Multiple outcome assessors
Cancian et al. (2013)	+	+	+	+	+	+	N/A
Matthews et al. (2007)	+	+	+	?	+	+	N/A
Braun et al. (2011)	+	+	+	+	+	+	N/A
Butler	+	+	+	?	?	+	N/A
Qian et al. (2011)	+	+	+	?	?	+	N/A
Gravelin et al. (2011)	+	+	+	+	+	+	N/A
Reingold et al. (2007)	+	+	+	?	?	+	N/A
Oujiri et al. (2011)	+	+	+	?	?	+	N/A
Warden et al. (2014)	+	+	+	?	?	+	N/A
Martinez et al. (2013)	+	+	+	?	?	+	N/A
Garin et al. (2012)	+	+	+	+	+	+	N/A
Whellan et al. (2001)	+	+	+	?	?	+	N/A

Fonarow et al. (2010)	+	+	+	?	?	+	N/A
Ghioghiarde et al. (2012)	+	+	+	?	?	+	N/A
Goff et al. (2005)	+	+	+	+	+	+	N/A
Riggio et al. (2009)	+	+	+	?	?	+	N/A
Scott et al. (2004)	+	+	+	?	?	+	N/A
Dykes et al. (2005)	+	+	+	?	?	+	N/A

+, criteria met; -, criteria not met; ?, unclear; N/A, not applicable

S5 Table: Contextual factors influencing implementation interventions among the included studies.

Study author, year	Contextual factors
Professional interventions	
Education	
Asch et al., 2005	Inner setting • *Leadership commitment*: Participating organizations demonstrated leadership commitment through a $125,000 contribution • *Mandate*: Intervention use was not mandated; following the training session, each organization was free to apply any implementation intervention they saw fit
Audit and Feedback	
Kasje et al., 2006	Inner setting • *Culture*: Most physicians were motivated to improve ACEI prescription • *Human factors*: Educational intervention was integrated into regular work flow Characteristics of individuals and teams • *Authority*: Primary care physicians were hesitant to change treatment initiated by a cardiologist
Cancian et al., 2013	Characteristics of individuals and teams • *Roles*: Limited primary care nurses; physicians dealt with most HF patients independently
Reminders	
Braun et al., 2006	Inner setting: • *Teams, networks, and communications*: In practices following the medical care centre model, primary care physicians and specialists shared the same equipment and rooms which promoted collaboration • *Culture*: Decision-making was considered a collaborative process
Butler et al., 2006	Outer setting: • *External policy and incentives/disincentives*: CMS was in the process of initiating public reporting of quality of care data Inner setting: • *Culture*: The research team was unable to effect cultural change to promote widespread adoption of the tool • *Mandate*: Intervention use remained optional (not mandated) during the intervention phase • *Human factors*: Intervention was designed to be unobtrusive

Qian et al., 2011	Outer setting: • *External policy and incentives/disincentives*: Reporting HF guideline-adherence data to TJC and CMS was mandatory Inner setting: • *Leadership commitment*: Leaders were involved in intervention planning
Gravelin et al., 2011	Outer setting: • *External policy and incentives/disincentives*: CMS reimbursed hospitals and physicians for appropriate ICD implantations
Professional interventions	
Changes in medical records systems	
Reingold et al., 2007	Outer setting: • *External policy and incentives/disincentives*: Implementation of computerized physician order-entry system was cited as a high national priority Inner setting: • *Culture*: Staff were committed to improving HF patient care • *Leadership commitment*: Emergency Department and Quality Improvement chairs released memos to encourage intervention use • *Measurement and data availability*: The team collected data on utilization of the intervention throughout the redesign process
Oujiri et al., 2011	Outer setting: • *External policy and incentives/disincentives*: TJC published performance measures for inpatient heart failure care Inner setting: • *Mandate*: Use of the implementation intervention was mandated for all hospital discharges • *Culture*: The intervention was well-received throughout the institution
Persell et al.,2011	Inner setting: • *Culture*: Staff were motivated to improve HF care
Clinical multidisciplinary teams	
Mejhert et al., 2004	Characteristics of individuals and teams • *Authority*: Nurses in program were allowed to institute and change the doses of medications
Martinez et al., 2013	Outer setting: • *External policy and incentives/disincentives*: CMS reduced reimbursement rates for hospitals with excessive HF readmissions

Clinical pathways	
McCue et al., 2009	Outer setting: • *External policies and initiatives*: TJC published performance measure for heart failure care
Financial interventions	
Provider incentives	
Esse et al., 2013	Outer setting: • *External policies and incentives*: The intervention was initiated by Medicare Advantage Prescription Drug Plan
Institutional incentives	
Lindenauer et al., 2007	Outer setting: • *External policies and incentives*: The intervention was developed collaboratively by the American Hospital Association, Federation of American Hospitals, and Association of American Medical Colleges.
Combined interventions	
Fonarow et al., 2010 Gheorghiadem et al., 2012	Inner setting: • *Mandate*: The use of provided resources was encouraged but not mandated; clinics were free to adopt/modify tools to their discretion
Goff et al., 2005	Outer setting: • *External policies and incentives*: State-wide quality improvement project with external funding to implement and evaluate the program
Riggio et al., 2009	Inner Setting: • *Leadership commitment*: Clinical Effectiveness Team that worked on developing the implementation intervention was chartered by the hospital's CEO and CMO Outer setting: • *External policies and incentives*: The Hospital Quality Initiative, launched by the US Department of Health and CMS, encouraged hospitals to report compliance with standardized performance measures. Better-performing hospitals were financially rewarded while poor performers were penalized. Hospitals in the study were at particular risk of financial penalty for non-compliance.
Scott et al., 2004	Inner setting: • *Leadership commitment*: Senior executives of state public health body were involved in the 2 year planning period preceding the intervention phase • *Culture*: Staff were motivated to improve HF

CMS, Centre for Medicare and Medicaid Services; TJC, The Joint Commission; CEO, chief executive officer; CMO, chief medical officer

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3-4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	4
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	4
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	4-5
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	5-6
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	S1 Appendix, S2 Appendix
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	5-6
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	6
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	6
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	6-7
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	N/A

PRISMA 2009 Checklist

Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency ($e.g., I^2$) for each meta-analysis.	7

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	N/A
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	N/A
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	10
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	12-25 (Table 3)
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	Supp. Tables S3-S7
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	11-26 (Table 3)
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	28-31 (narr. synth)
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	N/A
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	N/A
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	34-36
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	36-38
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	38-39
FUNDING			

PRISMA 2009 Checklist

Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	submission form

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097